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SYSTEMIC BACITRACIN IN THE TREATMENT OF PROGRESSIVE BACTERIAL SYNERGISTIC GANGRENE*

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IN 1926, THE ETIOLOGY of progressive bacterial synergistic gangrene was first clearly demonstrated by laboratory studies by one of us (F. L. M.) in connection with a case of Dr. George E. Brewer, and was reported in the ANNALS OF SURGERY.[1] It was found that far out in the spreading periphery of the lesion, a micro-aerophilic nonhemolytic streptococcus was present in pure culture and in the gangrenous margin it was associated with a hemolytic *Staphylococcus aureus*. In animals, it was demonstrated that these two organisms together were capable of producing a gangrenous lesion when combined, while neither alone in pure culture was able to produce any significant infection. This was later confirmed in 1931 in a similar fashion by laboratory studies in connection with a case of Dr. Richmond L. Moore's, again published in the ANNALS OF SURGERY.[2] Three more cases were described in 1933 and the differential diagnostic features between this disease and other types of infectious gangrene were described.[3]

The comparative rarity of this disease is probably due to the fact that the organism in the spreading periphery is one of relatively low virulence and the establishment of the infection depends upon the coincident presence of a staphylococcus capable of producing gangrene in tissue already inflamed by the nonhemolytic micro-aerophilic streptococcus. However, the disease is geographically widespread, because typical cases have been reported from North and South America, Europe, Asia and Australia. Well over 100

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cases have been described in the last 25 years and it is now thoroughly established as a clinical entity and should be promptly recognized by every surgeon of experience.

Routine bacteriologic studies have often failed to reveal the essential organisms, because it is necessary to use careful anaerobic cultural methods if the pin point colonies of the micro-aerophilic nonhemolytic streptococcus are to be found. Where a careful search has been made for this organism it has been recovered almost invariably and, unless such studies have been carried out, no one is entitled to question the findings of those careful bacteriologists who have used all of the methods necessary to demonstrate both aerobic and anaerobic bacteria. The cultural characteristics of these organisms have been fully outlined in the reports referred to above.[1, 2]

Certain authors have confused this clinical entity with other destructive lesions of the skin and subcutaneous tissues and in certain articles a heterogeneous mass of data has sometimes been collected under the term, "phagedenic ulcer." This is illustrated in a recent article by Dostrovsky and Sagher[4] in which it is obvious from the clinical course, the illustrations, and the bacteriologic findings that the article presents a wide variety of infections, including, to be sure, some cases of progressive bacterial synergistic gangrene. This is particularly unfortunate, because other authors have been trying to differentiate clearly clinical and bacteriologic entities among the various lesions, which in the past have been called phagedenic ulcers, a term which goes all the way back to Hippocrates and was used by many other authors long before precise bacteriologic methods were available.

It is true that in the early stages of this disease it may not be clearly differentiated from other skin infections or postoperative wound infections, but during the second or third week of its development it takes on certain clinical aspects which are unmistakable.

The chief symptom is the extraordinary pain and tenderness of the lesion. The gross appearance is characteristic. There is an outer zone of erythema varying from 1 to 10 cm. in width; inside of that a raised purple zone, the outer margin of which blends into the erythematous zone, while the inner margin is more sharply defined, crenated in outline, dark purple in color and is firmly adherent to a zone of gangrenous skin which has a typical suede leather, yellowish or brownish-green mottled, coloration and varies in width from 1 to 3 or 4 cm. The inner margin of the gangrenous zone is only slightly undermined, but it gradually melts away as the whole lesion spreads outwardly in all directions. The center of the lesion is a granulating ulcer, the granulations being of shaggy consistency, but as time goes on, this area may become bright red in color and relatively clean. The lesion is essentially a superficial infection and, as it spreads outward, it often leaves behind epithelial remnants of hair follicles or sweat glands which serve as the origin of regenerating epithelium.

The disease often starts in the skin around retention sutures which have been used to close, partially, an operative wound following the drainage of a

peritoneal abscess or an empyema. Very often the deep part of the wound closes while the characteristic gangrenous ulceration continues to spread on the surface. The disease is not always postoperative. Sometimes the lesion slowly develops around a colostomy or an ileostomy or in a trivial superficial accidental wound or in a skin lesion of long standing due to some other cause. Any break in the skin may permit secondary contamination with these organisms and, if they become established in the lesion, they may invade the surrounding tissues and produce the characteristic features of this clinical entity.

When the lesion has developed these characteristic symptoms and signs, there can be little doubt about the diagnosis. Thus, it has been possible to classify in this category many of the cases which have been reported in the literature on the clinical course alone, without the bacterial confirmation of the etiology but, unless the cases fit this clinical picture or unless the bacteriologic findings above mentioned are obtained, gangrenous infections of the skin should not be classified as cases of progressive bacterial synergistic gangrene and should be placed in other categories.

Until 1945 nothing had been found capable of bringing this infection under control except wide surgical excision. It is obvious from the nature of the pathology that the application of any local medication would be of no avail and, although a number of authors have stated that zinc peroxide has been recommended for this condition, such is not the case. Formerly, even excision frequently failed if the margin was not wide enough to remove all of the organisms spreading out from the periphery or if they became established again on the surface of the wound. Zinc peroxide has often been used successfully *after* excision to control any surface contaminants, but it has no place in the treatment of this disease without primary excision.

The sulfonamides have failed to change the course of this disease in any way, but, when penicillin became available, it was, of course, soon applied to this condition. Several favorable reports have appeared. The first included two typical cases reported by Meleney, Friedman and Harvey.[5] These cases responded so rapidly to penicillin that excision of the lesion was obviated. The erythema promptly disappeared, the raised purple zone flattened out and the gangrenous margin separated spontaneously. The defect was then covered with skin grafts. However, a third case of this kind, reported by these authors, which had multiple lesions developing spontaneously from trivial scratches, failed to respond to penicillin and it was demonstrated that one of the secondary contaminants of the *Ps. pyocyanea* group was present and actively produced a penicillinase, thus nullifying the benevolent action of penicillin at the site of the lesion. In this case, wide excision was necessary to control the infection, but the patient died later of pulmonary embolism. This casualty might have been avoided if bacitracin had been available at that time. The curative effect of penicillin in several other typical cases of progressive bacterial synergistic gangrene has been recently reported by Grimshaw and Stent in 1945,[6] by Canton in 1945–46,[7] by Cedarblade and Orr in 1946,[8] and by Clarke in 1947.[9]

Many of the reports of this disease have been simple descriptions of a single case and only very seldom has this clinical entity come into the experience of any individual surgeon more than once. However, a number of authors have attempted to collect all of the previously reported cases and excellent reviews have been made by Stewart-Wallace up to 1935,[10] by Dodd, Heekes and Geiser up to 1939[11] and by Meleney, Friedman and Harvey up to 1944.[5] Not included in the last review is a report by Hillenbrand and Brandt in 1943[12] which includes several cases of this disease mixed with other clinical entities and another authentic case observed by Gurruchaga and Manzoni in 1944.[13] Besides the four reports of cases treated with penicillin mentioned above, other typical cases have recently been described by Bassow in 1945,[14] by Martin and Cadiñanos in 1947,[15] by Cortese in 1947,[16] and by Lyall and Stuart in 1948.[17] This last report is of considerable interest because, while these authors confirm the synergistic etiology of the disease, they believe that *B. proteus* may be the synergist with the micro-aerophilic nonhemolytic streptococcus. In their first case they found these two organisms and failed to find a staphylococcus. Moreover, they were able to produce a lesion in animals when they combined the proteus and the streptococcus, but they could not produce any lesion with either organism in pure culture. While it is possible that in their first case the staphylococcus was masked by the proteus, the animal experiments carry considerable weight.

The present paper is written to record five typical cases of progressive bacterial synergistic gangrene, four of which failed to respond to penicillin but all of which yielded promptly to the systemic administration of bacitracin. In four of these cases we have demonstrated either that the organisms were resistant to penicillin or that there were secondary contaminants capable of producing penicillinase. Certain staphylococci, particularly those that are resistant to penicillin, are often able to produce penicillinase, as are many of the gram-negative aerobic rods and many strains of *Bacillus subtilis*, all of which are common contaminants of any open wound of long standing. It seems likely, therefore, that in the future there will be other cases similar to these that will require bacitracin or some other antibiotic when penicillin has failed, and it seems reasonable on the basis of these cases to recommend bacitracin as the primary treatment of choice.

CASE REPORTS

Case 1.—A. W., age 32 (Patient of F. L. M.; Hosp. No. 890692) was admitted November 17, 1947, and discharged January 14, 1948.

Four months before admission, this patient had been operated upon for fibroids of the uterus in one of the city hospitals. Retention sutures were used to close the abdominal wound, but, about the end of the first week, swelling and redness developed around the lower retention suture and the infection then gradually spread along the whole wound, which became extremely painful as the infection extended in all directions. The involved skin slowly became necrotic, leaving behind a shaggy ulcerated surface. It failed to respond to penicillin, streptomycin and sulfadiazine which were given systemically and to various agents which were used locally. Gradually the lesion took on the typical appearance of progressive bacterial synergistic gangrene. After two months of inexorable

spread, the surgeon in charge attempted to stop the progress of the disease by cutting a trench around it with the electric cautery. The trench was packed with gauze soaked with penicillin solution and for a time the infection seemed to be under control. Small skin grafts taken from the left thigh were applied to the central area, but they failed to take. A secondary closure of the trench was attempted, but infection promptly jumped the trench and spread out into the flanks and down both thighs. Four months after the onset of the infection, the patient was finally seen in consultation and a transfer to the Presbyterian Hospital was arranged (See Figs. 1, 2 and 3).

Physical Examination. The patient was a young colored woman with an extensive lesion involving the lower two-thirds of the abdomen extending out into the flanks on both sides and down both thighs. In the advancing margin on each thigh there was a

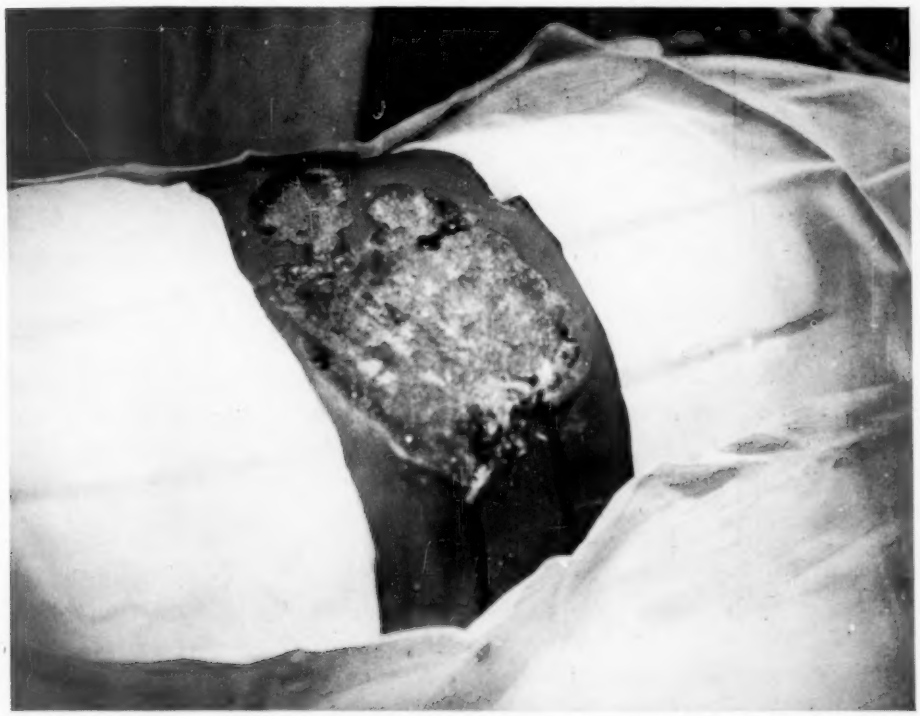

FIG. 1.—Case 1. The extent of the lesion after two months, showing the typical "suede leather" gangrene, the raised purple zone and the erythema around a part of the margin.

crescent-shaped area of suede leather gangrene, 3 to 4 inches long and about an inch wide, densely adherent to the surrounding skin, which was somewhat raised and purple in color. On the side of the skin toward the gangrene there was a sharp line of demarcation, but on the outer side the purple zone faded off into a zone of erythema, varying in width from ½ to 1 inch, but which was rather hard to discern through the pigmented skin. On the upper margin of the lesion on the abdomen, there was a narrower zone of frank gangrene, but a similar raised purple zone and an erythematous zone. The center of the lesion was made up of shaggy granulation tissue with here and there islands and areas of regenerating and degenerating epithelium.

Cultures were taken from various portions of the surface but not from the periphery of the lesion. The cultures were all overgrown with proteus, but, by means of a medium which partially inhibited the growth of this organism, a coagulase positive staphylococcus,

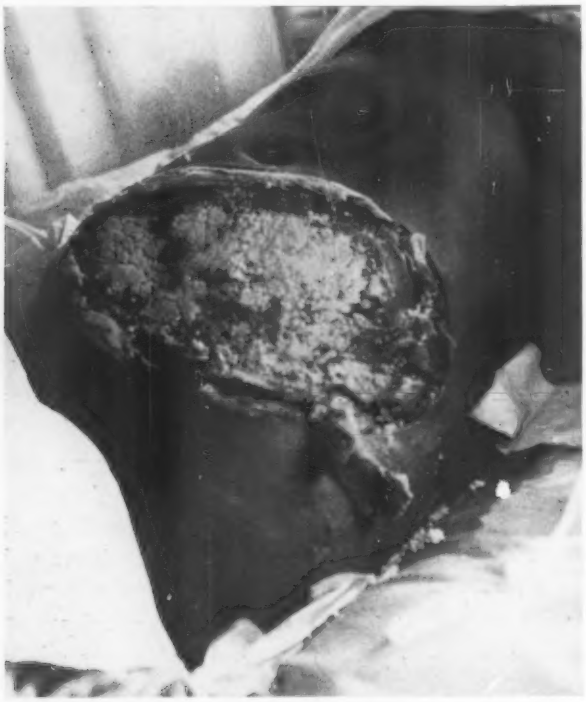

FIG. 2.—Case 1. Appearance of the lesion after two and one-half months. Attempt was made to control the infection by zinc peroxide and by cutting a trench packed with gauze soaked in penicillin.

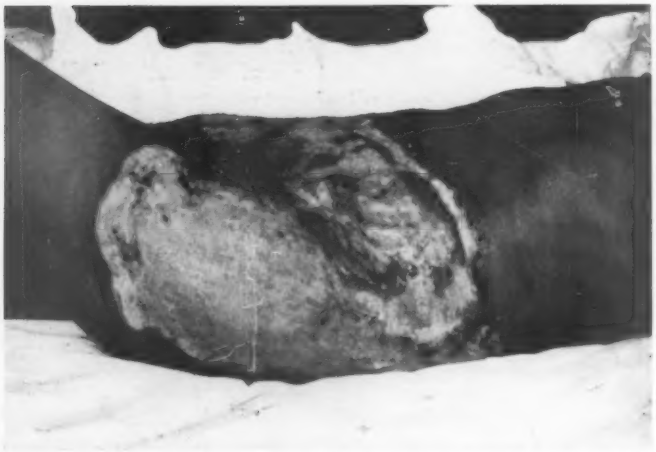

FIG. 3.—Case 1. Appearance of flank and left thigh when first seen by the senior author, four months after onset.

which was resistant to penicillin but susceptible to bacitracin, and a pyocyaneus, were found. Both the staphylococcus and the pyocyaneus demonstrated their ability to produce penicillinase, which offered an explanation for the failure of the infection to respond to penicillin. The micro-aerophilic nonhemolytic streptococcus was not found, as it might have been if cultures had been taken at the spreading periphery of the lesion. This is the first case of typical progressive bacterial synergistic gangrene in which it was impossible for our laboratory to find this essential organism, but the course and the clinical aspects of the case leave no doubt as to the diagnosis.

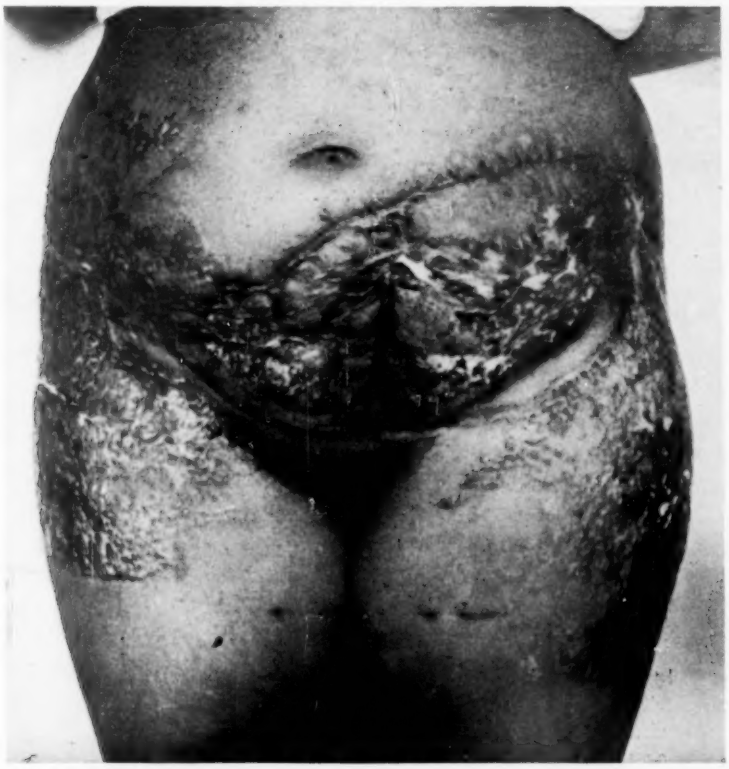

FIG. 4.—Case 1. Complete healing of lesion seven weeks after starting bacitracin.

Course. The patient was given 20,000 units of bacitracin intramuscularly every 6 hours. Bacitracin was also used locally in a concentration of 1,000 units per cc. on a single layer of fine meshed gauze kept moist by a double layer of zinc oxide ointment gauze. There was a dramatic improvement in the patient's general condition as well as in the local lesion in 48 hours. The erythema promptly receded. The purple zone flattened out and the gangrenous skin on the right thigh became loose and detached from the purple zone and it was easily lifted off as a plaque. On the third day, the gangrenous skin on the left thigh was similarly removed without the necessity for cutting. The whole lesion very rapidly took on a benign appearance, the margins flattened down and the exudate became less. Within a week, it was clearly obvious that new epithelium was growing with great rapidity from residual islands all over the surface of the lesion, in spite of the fact that gram-negative rods were present which were not affected by the bacitracin. However, in order to hasten healing by the inhibition of the activity of these organisms.

0.25 per cent of parachlorophenol was added to the bacitracin solution for local application to the surface by means of fine meshed gauze.

After that the whole area rapidly became completely epithelialized. The later stages of epithelialization were hastened by the local application of 2 per cent oxyquiniline in 5 per cent scarlet red ointment. Healing, therefore, did not require either excision or skin grafting. Convalescence was complicated by an intercurrent intestinal infection with *Salmonella montevideo* which caused a diarrhea with high fever and a septicemia, but this halted the healing process only temporarily. Other patients in the ward suffered from this infection at the same time and it was evidently due to food contamination. There was no evidence of toxicity from either the local or the systemic bacitracin which was continued for 30 days for a total dosage of 2,160,000 units systemically and 357,000 units locally (See Fig. 4).

This case clearly demonstrates the efficacy and safety of systemic bacitracin in the treatment of progressive postoperative bacterial synergistic gangrene, obviating the necessity for surgical excision or skin grafting, after the failure of penicillin, streptomycin and sulfadiazine in large doses over a period of four months. Bacitracin was not inhibited by the staphylococcus or the secondary contaminant, *Ps. pyocyaneus,* which were not only resistant to penicillin but which were both capable of producing penicillinase. This result could not have been obtained by the local application of any medication, for it could not hope to reach the spreading border of the lesion. It, therefore, must be assumed that the systemic drug was chiefly responsible for bringing the infection under control.

Case 2.—D. R., age 44 (Patient of F. L. M.; Hosp. No. 904634) was admitted March 30, 1948, and discharged April 21, 1948.

This patient had had chronic ulcerative colitis off and on for a period of 15 years, but this was held under fair control by diet. Five weeks before admission to the hospital, she had a slight abrasion on the front of her right leg. This became infected and an ulcer formed which gradually spread downward toward the ankle, then posteriorly and then up the calf toward the popliteal space, with an advancing zone of erythema and a progressive death of skin. The process advanced insidiously in spite of large doses of penicillin, streptomycin and sulfadiazine and various and sundry local applications, all of which had no effect, but, as the lesions spread outward, there was some evidence of regenerating epithelium in the central portions which were otherwise covered by granulation tissue. The pain had been so great that she had not had a good night's sleep since the onset of the infection.

Physical Examination. The patient was a poorly nourished, thin, anemic woman in great pain and anxiety. The right leg was almost completely surrounded by an extensive ulcer extending from the ankle up to the popliteal space and involving about three-fourths of the circumference of the leg, leaving only a narrow zone of uninvolved skin at the front. Around most of the margin there was a zone of gangrene which was widest on the calf just below the popliteal space. The zone of erythema was of varying width extending well up into the popliteal space where the spread seemed to be most active. The central portion of the lesion was covered with granulation tissue with some irregular islands of regenerating and degenerating epithelium. The whole area was stained irregularly with gentian violet, the last of the ineffective local medications to be applied. Cultures taken from beneath the gangrenous margin revealed the micro-aerophilic nonhemolytic streptococcus and the *Staphylococcus aureus* characteristic of the bacteriology of progressive bacterial synergistic gangrene. The streptococcus was sensitive to both bacitracin and penicillin, while the staphylococcus was sensitive to bacitracin but resistant to penicillin.

Course. The patient was very apprehensive and soon after her admission she began to have a diarrhea which she said indicated a reactivity of the colitis. She was given bacitracin in a dosage of 24,500 units every 6 hours intramuscularly and because of the diarrhea 5,000 units of bacitracin were administered by mouth four times a day. Bacitracin was also used locally on fine meshed gauze in a concentration of 500 units per cc. This was covered by a double layer of gauze impregnated with zinc oxide ointment to keep the dressing moist. Improvement was evident within 48 hours. The erythema faded rapidly and the raised purple zone flattened out and its color improved. The gangrenous skin began to separate from the purple zone and from the tissue beneath it. The islands of epithelium at the center began to regenerate at their margins. In a week's time, all of the dead skin had separated and the area was half covered with new skin. During the first week, the colitis subsided completely. After two weeks, the epithelium had covered all but an area two inches in diameter at the upper part of the calf. Final epithelialization was complete when the patient went home on the twenty-second day. The urine showed a transient albuminuria and cylindruria, but blood studies showed no elevation of the nonprotein nitrogen or the urea nitrogen. Phenolsulphonphthalein elimination was 80 per cent in two hours at the end of treatment. Systemic bacitracin was continued for 18 days for a total of 1,715,000 units; 78,000 units were used locally and 415,000 were given by mouth. (It is not absorbed to any great extent from the gastro-intestinal tract, where it is retained and inhibits the growth of susceptible organisms.)

This case illustrates the prompt response to systemic and local bacitracin of a typical case of progressive bacterial synergistic gangrene resulting from the establishment of the characteristic bacterial species in an abraded wound. Penicillin, streptomycin and sulfadiazine had all failed to control the infection and, because of its nature, we must assume that it was the systemic rather than the local bacitracin which halted the progress of the infection. Possibly the systemic as well as the mouth medication helped to control the associated colitis.

Case 3.—F. B., age 57 (Patient of F. L. M.; Hosp. No. 749989) was admitted April 20, 1948, and discharged July 1, 1948.

The patient had suffered from mycosis fungoides for a number of years with lesions all over his body, particularly on the feet. The involved areas usually developed slowly with localized swelling and redness and then dissolution of the overlying skin would follow with or without blistering. The diagnosis had been repeatedly confirmed by biopsy. These lesions frequently became infected, but this feature was of minor importance and was generally controlled by simple local medication. On one of these occasions, he was given penicillin by mouth and penicillin ointment locally, but it had to be discontinued because of penicillin allergy. About two months before admission to the hospital, however, an area of gangrene developed on the side of the right foot and the surrounding tissue became acutely inflamed and swollen. This area slowly enlarged and gradually took on the characteristic appearance of progressive bacterial synergistic gangrene with a zone of densely adherent necrotic skin surrounded by a raised purple zone with a surrounding fiery red erythema. The whole area became extremely tender and painful and the patient's attending dermatologist then referred him to the hospital for the control of the infection.

Physical Examination. The patient was well developed and nourished, but in considerable pain from the lesion on his foot, which extended from the bases of the toes up to the front and outer side of the ankle. There were two areas of adherent suede leather gangrene connected by a narrow strip of ulcerated skin with a raised purplish margin (Fig. 5). The whole area was swollen and surrounded by a cellulitis, the erythema extending in all directions, particularly toward the inner side of the foot. On the sole were several areas of mycosis fungoides not involved in the gangrenous process. Cultures

from the lesion revealed the micro-aerophilic nonhemolytic streptococcus and the coagulase positive *Staphylococcus aureus,* both susceptible to penicillin and bacitracin, as well as *Ps. pyocyaneus.*

Course. The patient was given bacitracin in a dosage of 19,000 units every 6 hours and the local lesion was dressed with a carbowax (water soluble) ointment containing 500 units of bacitracin per gram with a quarter of one per cent parachlorophenol to take care of the pyocyaneus. Improvement was striking. The cellulitis and erythema subsided promptly. The dead skin separated at the margins and after three days it was possible to peel it off from the underlying tissues. New skin then began to grow in from the margins and from residual islands of epithelium. The cocci disappeared promptly, but the pyocyaneus persisted for some time in the culture. Healing then took place slowly. The pyocyaneus gradually disappeared from the wound and the lesions of mycosis fungoides responded to small repeated doses of roentgen radiation.

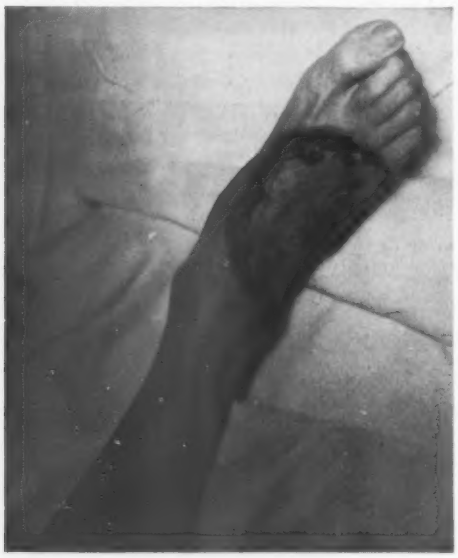

FIG. 5.—Case 3. Appearance of the lesion when first seen by the senior author, showing the "suede leather" gangrene, the raised purple zone and the erythema.

Urinalysis was normal and the N. P. N. was 26 mg. per 100 cc. before starting bacitracin, but gradually albumin, casts and cellular elements appeared in the urine. The N. P. N. rose to 43 mg. per 100 cc. and the P. S. P. fell from 70 per cent to 35 per cent. It did not seem necessary to stop treatment, but the lot was changed on the eleventh day from No. 480120 to No. 480210. On the next day, a rash appeared across the shoulders and gradually spread all over the back and chest with a few areas on the arms. Therefore, the infection having been controlled, it was decided on the twelfth day to stop the systemic bacitracin but continue it locally. The rash slowly subsided following benadryl and pyribenzamine. The N. P. N. promptly returned to normal and the P. S. P. rose again. A later study of toxicity of various lots of bacitracin showed that the ones used in this case were among the most toxic, but they were clinically effective and the evidences of kidney irritation or damage were promptly reversible. (Considerably less toxic lots are now available.)

This case illustrates the development of progressive bacterial synergistic gangrene following the contamination of the lesions of mycosis fungoides with the essential organisms of this synergistic infection. After other treatment had failed, the infection promptly responded to bacitracin and, although this manifested some side effects of nephrotoxicity, they were transient and did not interfere with the clinical effectiveness of the drug.

Case 4.—L. H., age 42, a patient of P. S., Illinois Masonic Hospital No. 99355, was admitted January 19, 1948, and discharged April 27, 1948.

This patient had been suffering for six months with a bloody diarrhea which had resulted in a weight loss of 50 pounds and a progressive cachexia and anemia. Colonic roentgen rays showed a typical advanced ulcerative colitis. No amebas were found in the

stools. Daily spikes of fever ranged from 100° to 102°. She made no response to a strict dietary regimen over a period of one month in the hospital and ran a progressively downhill course. Then a double-barrelled ileostomy was performed and resulted in slight improvement in her general condition, but a profuse muco-purulent rectal discharge continued and the patient developed a progressive hypoproteinemia which could not be controlled by repeated blood and plasma transfusions and various intravenous and per os protein hydrolysates. Her weight remained around 110 and her legs became progressively edematous. The skin about the ileostomy remained in good condition for several weeks and then began to show small superficial breaks in the surface, which soon showed signs of infection. This resisted all efforts to control it. Finally, 8 weeks after the ileostomy, an infection started on one side of the stomata with swelling and redness and discoloration of the skin. This went on rapidly to a spreading necrosis with all of the characteristic features of progressive bacterial synergistic gangrene, extending outward from the stomata in all directions. Almost simultaneously, similar gangrenous areas developed in the right flank and on the right leg just above the ankle. The lesions were characterized by extreme pain and tenderness and rapid spread and the patient's morale began to fail rapidly. Penicillin in large doses, sulfadiazine, and streptomycin were tried systemically to no avail, while zinc peroxide, tyrothrycin, penicillin and azochloramide were used locally without benefit. Finally, the surgeon in charge called for bacitracin.

Physical Examination. The lesions showed all of the typical features of progressive bacterial synergistic gangrene. Around the ileostomy stomata the lesion measured 4 by 5 inches, in the flank 2 by 3 inches and on the leg 5 by 6 inches. In each area there was a central ulceration with boggy granulations covered by a purulent exudate. Around this was a zone of yellowish black gangrenous skin surrounded in turn by a raised purple zone and beyond that an erythema of variable width. Cultures from the ulcerated areas revealed a coagulase positive *Staphylococcus aureus,* susceptible to bacitracin but resistant to penicillin. The laboratory reported that the anaerobic cultures showed no growth, but this must have been an error because the staphylococcus, if present aerobically, would certainly have grown on the anaerobic plate or in anaerobic broth and might well have masked the smaller colonies or the slower growth of the micro-aerophilic nonhemolytic streptococcus.

Course. When bacitracin was made available, the patient received 24,500 units intramuscularly every 6 hours and this was continued for 11 days, for a total of 1,078,000 units. The progress of the infection came to a standstill in 48 hours. The gangrenous skin soon began to separate spontaneously, the raised purple zone flattened out and the erythema progressively diminished. The exudate became scanty and the granulations took on a firm consistency and a bright red color. The areas on the abdomen and flank were covered with "pinch" grafts on the twelfth day and the ankle on the fourteenth. These grafts rapidly fused and covered the areas with new skin.

After stopping the systemic bacitracin, the rectal purulent discharge, which had markedly diminished during treatment, recurred. Bacitracin was then introduced into the distal ileostomy stoma in solution form in a dosage of 5,000 units once a day. The purulent character and the quantity rapidly diminished and the patient's general condition and morale steadily improved.

This case illustrates the development of the typical lesion of progressive bacterial synergistic gangrene around an ileostomy in a case of chronic ulcerative colitis and two simultaneous similar lesions on other areas of the body, which failed to respond to penicillin in large doses, sulfadiazine and streptomycin, but which were controlled within 48 hours by systemic bacitracin. The gangrenous skin separated spontaneously and the resulting ulcer rapidly prepared itself to accept skin grafts, which readily took hold and covered the

defect. At the same time, the ulcerative colitis cleared rapidly, first under the systemic treatment and again under the local administration of bacitracin.

Case 5.—M. B., age 34, a patient of R. S. M. at North Country Community Hospital, Glen Cove, L. I., No. 64452, was admitted November 15, 1948, and discharged December 13, 1948.

The patient was admitted at term in mild labor of one hour's duration. There had been a long record of infertility. Her antepartum course had been relatively uneventful.

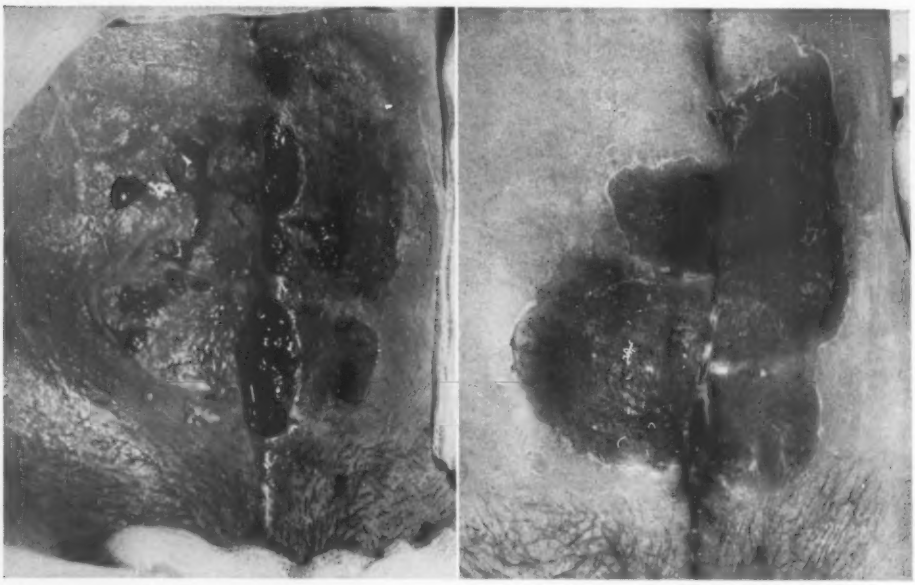

FIG. 6 FIG. 7

FIG. 6.—Case 5. Appearance of the lesion on its ninth day, just after starting bacitracin, showing the early characteristic features of the disease, a carbuncular appearance with a raised bluish-purple zone of necrobiotic tissue.

FIG. 7.—Case 5. Appearance of the lesion ten days after starting bacitracin, showing complete resolution of the process without any death of the skin and with rapid healing.

After six hours of moderate contractions, the membranes ruptured and good hard labor ensued. After 13 hours, the cervix was three fingers dilated. The following three hours of strong uterine contraction produced no progress. The fetal heart became accelerated and, in view of the low index of fertility, a cesarean section was deemed advisable. The patient was given 60,000 units of penicillin in distilled water intramuscularly prophylactically. A cesarean section was performed without difficulty through a low midline abdominal incision and a transverse low flap uterine incision. Two grams of sulfanilamide crystals were sprinkled underneath the bladder flap after closing the uterine incision. The abdomen was closed in layers with catgut. Four silk stay sutures were inserted and threaded through rubber tubing.

Following the operation, 40,000 units of penicillin were administered intramuscularly every 3 hours for 6 days; and 7 hours after the operation, 1 Gm. of sulfadiazine, in combination with 2 Gm. of soda bicarbonate, was given orally every 4 hours for 3 days. On the second postoperative day, the patient was allowed out of bed. Her postoperative course continued satisfactorily until the eighth postoperative day, at which time exam-

ination of the abdominal wound revealed small vesicles lateral to the ends of each piece of rubber tubing, underneath the stay sutures, such as one would see in a second degree burn. It was considered at this time that the patient was probably sensitive to the rubber and was having an allergic skin reaction. The tubing was cut out, leaving the stay sutures in place. Twenty-four hours later the vesicular areas had spread so as to almost join each other in the midline and there was some redness along the wound edge, indicative of a secondary infection. Penicillin was resumed on the twelfth postoperative day. Cultures of the wound taken at this time revealed *E. coli* when read 48 hours later. On this account, penicillin was stopped and streptomycin was given in combination with sulfadiazine, but they had no effect. The entire wound became inflamed. The wound margins separated for a width of about 2 cm. and a depth of 1 to 1½ cm. All along the wound surface there was a purulent exudate and a dusky swelling appeared around the retention sutures, especially at the upper part of the wound on the left side. It was obvious that this represented the earliest changes seen previously in typical cases of progressive bacterial synergistic gangrene and it became of considerable importance to stop the process before it could result in extensive death of skin. Penicillin and sulfadiazine both had failed as prophylactics and penicillin, streptomycin and sulfadiazine had failed to stop the infection after its onset. Additional cultures confirmed the diagnosis by revealing a hemolytic *Staphylococcus aureus*, resistant to penicillin but susceptible to bacitracin, and a micro-aerophilic nonhemolytic streptococcus. *Escherichia coli* and aerobacter were also present. These species are both capable of producing penicillinase, although this effect was not demonstrated for these organisms *in vitro* (See Fig. 6).

Course. On the sixteenth postoperative day and on the eighth day of the infection the stay sutures were removed and bacitracin was given in a dosage of 10,000 units every 6 hours intramuscularly. It was applied locally on wet compresses in a concentration of 1,000 units per cc. The dressings were kept moist by the application of zinc oxide ointment gauze. The photographs taken on the seventeenth postoperative day illustrate the status of the wound 24 hours after medication was instituted, at which time there was already some improvement. Additional photographs taken at the end of ten days revealed the wound closed except for a small area measuring about ¼ cm. (See Fig. 7).

During the administration of the bacitracin, daily checks were made on the patient's urine, nonprotein nitrogen and phenolsulphonphthalein tests. The patient developed three plus albumin in her urine on the fourth day following administration of bacitracin, but this gradually decreased during treatment. Urinalysis and blood chemistry taken after the patient's discharge from the hospital were normal.

This case illustrates the development of progressive bacterial synergistic gangrene in a cesarean section wound made after the rupture of the membranes, the organisms probably coming from the vagina. It developed in spite of the prophylactic use of penicillin and of sulfadiazine both locally and systemically, probably because of the associated Gram negative rods. After its development, it failed to respond to penicillin, sulfadiazine and streptomycin. Its nature was recognized early before there was extensive death of skin. Its progress was promptly arrested by the systemic administration of bacitracin. Surgery was obviated and rapid resolution of the process resulted.

COMMENT

The five cases included in this report all showed the characteristic clinical features of progressive bacterial synergistic gangrene. In two of these cases, the micro-aerophilic nonhemolytic streptococcus was not found, but we believe

this was due to the fact that no cultures were taken from the spreading zone of erythema and this organism was probably overgrown by secondary contaminants in the area of gangrene and ulceration. The failure to find this organism does not, therefore, rule out the diagnosis.

Only two of these five cases, the first and the last, were postoperative infections in the usual sense. In Case 4 the lesion developed around an ileostomy eight weeks after operation while two other lesions developed away from the operative site at the same time. Case 2 produced the lesion in a simple abrasion, while in Case 3 the disease followed the contamination of an area of mycosis fungoides. For this reason, the authors feel that the name "progressive bacterial synergistic gangrene" should be retained and used for this clinical entity, but that the word "postoperative" should only be added in those cases in which it develops within the first two or three weeks after operation in the true sense.

Four of these cases failed to respond to penicillin and it was not used in the other case because it had been previously demonstrated that the patient was allergic to penicillin. The failure of penicillin can probably be explained either by the fact that the organisms present were resistant or were capable of producing penicillinase. All of these cases responded promptly to bacitracin and the nature of the infection makes it certain that the systemic administration of bacitracin rather than its local use was largely responsible for this control. In each case the staphylococcus and, where it was found, the microaerophilic nonhemolytic streptococcus were susceptible to bacitracin. It would seem, therefore, that bacitracin rather than penicillin is, at present, the treatment of choice in this disease.

In all of these cases, surgical excision was obviated and, if other similar cases respond in the same way, we believe that excision either with the knife or with the cautery is no longer indicated nor should any attempt be made to stop the infection by cutting a trench around it. In only one of these cases was it necessary to cover over the defect with skin grafts, because in all of the other instances the defect was restored by the growth of epithelium from the residual islands that had been left in the outward spread of the gangrenous process.

In only one of these cases was there any evidence of toxicity from the drug and this was only of moderate severity and short duration and did not interfere with the curative effect of the drug. It was later found that the lots that were used in this particular case were both of relatively high toxicity when compared with the lots used in the other cases and with the product that is now available for systemic use.

The last case demonstrates that this disease can be diagnosed in its early stages both by the characteristic clinical features and by bacteriologic studies. Certainly, as soon as it has formed its characteristic zones by the end of the third or fourth week of its course, it should be recognized by everyone and the proper treatment should be administered. Bacitracin should be started in a dosage of 400 units per kilogram of body weight every six to eight hours.

The urine should be examined every day for albumin, casts, white cells, red cells and epithelial cells and the B. U. N. or N. P. N. should be taken every third day. The presence of albumin or casts in the urine does not require a termination of treatment unless they should reach serious proportions, because it may be expected that they will diminish during the course of treatment or immediately after its termination.

SUMMARY

Five more cases of progressive bacterial synergistic gangrene have been presented herewith, all of which responded promptly to systemic bacitracin after they had failed to respond to other methods of treatment. Four of these had had penicillin without benefit. In the other case, penicillin had not been used because of the previous demonstration of an allergic response.

This series of cases illustrates the disease from its earliest development, when it was recognized at an early stage before extensive destruction of skin, to a very late stage in which, after four months, it had involved all of the lower abdomen, the flanks and the upper portions of the thighs.

All of these cases showed the typical clinical symptoms of progressive bacterial synergistic gangrene and the essential organisms were found in three. In the other two cases, the micro-aerophilic nonhemolytic streptococcus escaped recovery, probably due to the overgrowth of secondary contaminants.

These cases clearly indicate that systemic bacitracin is today the treatment of choice for this clinical entity.

The authors appreciate the careful bacteriologic studies made by Miss Balbina Johnson in connection with Cases 1, 2, 3 and 5.

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CHRONIC RELAPSING PANCREATITIS
TREATMENT BY SUBTOTAL GASTRECTOMY AND VAGOTOMY*

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NUMEROUS REPORTS in recent literature have served to emphasize the increasing recognition of chronic inflammatory lesions of the pancreas. This is probably due to better methods of diagnosis and to an increasing appreciation of the existence of the disease. None of the more commonly used textbooks of medicine devotes more than a few lines to a description of this condition, and it remained for Comfort, Gambill and Baggenstoss[1] in 1946 to clarify the disease picture, as we now recognize it. They re-introduced the descriptive term "chronic relapsing pancreatitis," a name which is well chosen since the condition is an inflammation of the pancreas characterized by periods of exacerbation separated by variable intervals of remission. There are recurrent acute painful episodes, often severe enough to incapacitate the patient for long periods of time and to warrant urgent medical attention. Intervals of minimal or even absent symptomatology are apt to follow.

The therapeutic approach to chronic relapsing pancreatitis involves a knowledge of the underlying etiologic and pathologic factors, and encompasses varied medical and surgical methods. The purpose of this report is to review the pathologic features of the disease and to emphasize its clinical aspects. The case histories of three patients will be presented. They were treated by subtotal gastrectomy in an attempt to correct partially the abnormal physiologic mechanism involved in the production of the disease.

PATHOLOGIC CONSIDERATIONS

In this discussion of chronic relapsing pancreatitis, only those pathologic phases will be considered which appear germane to the subject. Chronic pancreatitis represents the summation of repeated attacks of acute pancreatitis.

Bacterial infection of the pancreas may produce the typical picture of acute pancreatitis. This has been proved experimentally and clinically.[2] The theory of lymphogenous spread of infection to the pancreas, which at one time held sway in discussion of the etiology of pancreatitis, assumed that infection occurs by ramification through the anastomosing network of lymphatics in the retroperitoneal tissue which connects the gallbladder with the pancreas. This theory has been disproved by the work of Kodama[3] who was unable to demonstrate such direct lymphatic connection. Wangensteen and his co-workers,[4] after clinical and laboratory investigations, have concluded that lymphogenous spread is rarely, if ever, responsible for acute pancreatitis.

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Uncommon causes for acute pancreatitis are external trauma, and vascular accidents such as arterial embolism and thrombosis. Infectious diseases, notably typhoid fever, scarlet fever and mumps, may be responsible for the acute disease.

The reflux of bile, high in its concentration of bile salts, and in its content of pathogenic bacteria, is undoubtedly an important factor in the destruction of pancreatic tissue. The presence of bile in the pancreatic duct, as well as that of pancreatic ferments in the choledochus predicates the existence of an ampulla of Vater guarded by the ampullary muscle. Obstruction of the ampulla either by spasm, edema or a biliary calculus, may convert the common bile duct and the pancreatic duct into one common canal. The incidence of the anatomic variations of the sphincter mechanism has been the subject of much discussion.[5-9] Dragstedt, Haymond and Ellis[10] summarized the literature in 1934, and in conjunction with their own experiences, came to the conclusion that a common channel may be created in about 60 per cent of cases, but that in only 10 per cent of these does an impacted stone convert the two ducts into a common channel. They felt that pancreatitis was caused by the reflux of infected bile into the pancreatic ducts.

However, it has been shown[11] that, even where a common channel exists, pancreatitis does not necessarily develop. The pancreatic duct was visualized in seven, or 20 per cent of 35 cases upon whom cholangiograms were done during a period of postoperative drainage of the common bile duct. None of these seven patients developed pancreatitis, even though bile must have been present along with the lipiodol in the pancreatic duct.

Rich and Duff[12] in 1936, offered an explanation for those cases of pancreatitis, in which biliary disease was not a factor. They demonstrated that metaplastic changes in the epithelium of the pancreatic duct could produce an obstruction to the flow of pancreatic juice. If the obstruction was severe enough, and the pressure of pancreatic secretion sufficiently elevated, rupture of some of the smaller ducts might ensue. The extravasation of pancreatic juice into the parenchyma with activation of trypsinogen into trypsin, might result in digestion of pancreatic tissue. They were able to substantiate this point experimentally and called attention to the fact that many cases of acute pancreatitis follow an alcoholic bout or a heavy meal, at which time pancreatic secretion is at its height.

Myers and Keefer[13] thought that alcoholism could cause an acute congestion of the duodenum which might lead either to obstruction of the duct orifices, or in some cases to ascending infection. They suggested that episodes of vomiting might cause regurgitation of the duodenal contents into the pancreatic ducts, with subsequent activation of the pancreatic ferments.

Several investigators have been able to produce varying stages of acute pancreatitis in animals. Popper and Necheles,[14] after partially ligating the pancreatic ducts, administered secretin and produced extensive edema of the pancreas. Reasoning from these observations, they concluded that in man, pancreatitis may follow a heavy meal as a result of the activation of secretin

in the presence of obstruction of the ducts of Wirsung and Santorini. Lium and Maddock[15] performed similar experiments, partially ligating the ducts and stimulating pancreatic secretion by secretin, pilocarpine, and acetylbeta-methyl-choline, and by the administration of a meal high in fat. They were able to produce changes varying from mild inflammation to dissolution of pancreatic tissue. As a result of their experiments, they concluded that pancreatitis may result from an actively secreting pancreas in the presence of obstruction.

The sequence of events in pancreatitis in human beings can be translated in the light of these experimental findings. If the degree of obstruction is slight, and the secretin stimulus moderate, edema of the pancreas may result when pancreatic juice diffuses through the wall of a duct whose permeability has been altered by the increased pressure. If the obstruction is more marked and the secretory pressure elevated, the finer ducts may rupture. The liberated proteolytic enzyme, trypsinogen, is activated, resulting in pancreatic edema, hemorrhage and necrosis. Varying degrees of these three processes may occur simultaneously in different portions of the gland.

As the acute inflammation subsides following each attack, the pancreas becomes indurated and nodular due to fibrosis of, and calcium deposition within the necrotic areas. Atrophy is often marked, although occasionally at operation the pancreas may be enlarged and swollen. Fatty infiltration and pseudocysts may be evident. A pancreatic abscess may develop if infection supervenes during the recovery period. In addition to the calcification and fibrosis, which may be severe, atrophy of the acini and the islets of Langerhans is often seen. Lymphocytes, plasma cells and eosinophils are present. The epithelium of the ducts, whose diameter is lessened, may show metaplasia. The lumen may contain inspissated material, and occasionally calcium. Naturally the quantity of pancreatic juice is diminished.

CLINICAL CONSIDERATIONS

Predisposing factors in patients with chronic pancreatitis, aside from the definitive history of an acute attack, occasionally proved by operation, are a history of alcoholism and pre-existing biliary tract disease. Comfort *et al.*[1] reported that 17 out of 25 patients admitted using alcohol to excess. Weiner and Tennant[16] noted the association of acute alcoholism in 27, or 52 per cent of 51 cases of acute pancreatitis, and chronic alcoholism in 19, or 47 per cent of 41 cases of chronic pancreatitis which came to autopsy. Clark[17] observed 27 cases of acute and chronic pancreatitis in 150 necropsies of patients with alcoholic histories. Myers and Keefer[13] reported alcoholism in 17 or 33 per cent of 51 cases of pancreatitis. Two of the three cases herewith reported were given to excessive drinking.

There is a plausible explanation for this association of alcoholism and pancreatitis. Alcohol, in its contact with the duodenal mucosa, causes the formation of excessive secretin. The latter stimulates the production of a large quantity of pancreatic juice. If this meets with obstruction in the form

of edema of the duodenal mucous membrane, or narrowing of the pancreatic ducts by metaplasia or calcification, pancreatitis may result.

Following cholecystectomy, many patients suffer from a train of symptoms known as the post-cholecystectomy syndrome. In the majority, this may be ascribed to a temporary dyskinesia of the sphincter mechanism. In most instances the symptoms disappear within one to two years. If the episodes persist, surgical exploration will reveal either organic causes, or, in the absence of definite pathologic changes, an intractable dyskinesia of the sphincter must be assumed. Some observers have stated that in many of these patients the attacks are due to the repeated insult of a biliary reflux, resulting eventually in a chronic pancreatitis.

It is rather interesting to note that Dreiling and Hollander[18] did secretin studies in 67 cases of post cholecystectomy syndrome, and in none of these was there any evidence of a lowering of either the bicarbonate concentration or amylase content of the pancreatic juice. While it is undoubtedly true that biliary reflux plays an important role in the etiology of some cases of chronic relapsing pancreatitis, many cases can not be attributed to this factor. In such instances, the pathology may be found within the pancreas and in disturbance of the secretin mechanism.

The clinical picture of chronic relapsing pancreatitis is characterized by repeated attacks of pain of varying intensity, and dyspeptic symptoms, such as nausea, heartburn and belching. Occasionally, pruritus due to associated icterus, is a symptom. In many cases, frequent bulky movements are noted, and this may be the first evidence of the development of pancreatic insufficiency. Steatorrhea and creatorrhea are the expression of loss of pancreatic ferments with deficient digestion of protein and fat, resulting in diarrhea, loss of weight and weakness. Diabetes mellitus develops when the destructive processes involve the islets of Langerhans, and this likewise contributes to the generalized debility.

The physical examination of these patients reveals abdominal tenderness, weight loss, and occasionally jaundice. In rare instances, a pancreatic cyst may be palpated abdominally. In one of our patients, the calcified pancreas could be felt through a thin abdominal wall.

The secretin test of pancreatic function in chronic relapsing pancreatitis as reported by Dreiling and Hollander,[19] showed that the response is abnormal in that bicarbonate concentration is lowered markedly and consistently. The amylase content and volume of the pancreatic juice are also diminished, although not to so marked an extent as the bicarbonate concentration.

Blood amylase tests have shown no significant findings except where the pancreas is markedly fibrotic. Here, as one would expect, the enzyme content is very low. During the acute exacerbations, elevations of blood amylase, if present, are of great diagnostic value. Sugar tolerance tests may reveal a diabetic curve even before glycosuria and hyperglycemia are evident. Chemical examination of the stool discloses a high percentage of fat content, over 40 per cent (normal 8 to 25 per cent).

Roentgen ray studies reveal varying degrees of calcification in about 33 per cent of the cases. If enlargement of the pancreas is present, barium meal studies may reveal displacement of the antrum and body of the stomach and widening of the duodenal curve. Occasionally, a small bowel deficiency pattern is encountered. Stenosis of the colon[20] and a portion of the small bowel have been reported.

TREATMENT

The treatment of chronic pancreatitis is far from standardized. Medical therapy which is usually unsatisfactory, includes a high caloric, high protein, low fat diet supplemented by vitamins. Carbohydrate restriction and insulin are necessary if diabetes mellitus is present. The total caloric intake is divided into several small meals to minimize secretin formation, and possible overloading of the pancreatic ductal system by increasing pancreatic secretion. Alcohol and tobacco are interdicted, the former for its secretin effect, the latter for its possible effect on the autonomic ganglia supplying the pancreas. Substitution therapy includes Pancreatin (8 to 20 Gm.) daily in all cases, and insulin, when diabetes is present.

In cases in which the gallbladder has been removed, measures should be instituted which will favor a periodic relaxation of the common bile duct and pancreatic sphincters, or the peri-ampullary muscle, if present. These have been fully discussed elsewhere. The biliary flush regimen suggested recently by Best[21] should prove helpful. All these measures aim to maintain a normal pressure relationship within the biliary and pancreatic duct systems by a periodic relaxation of the sphincters.

For the most distressing symptom, pain, a sedative antispasmodic mixture such as atropine, gr. 1/150, and phenobarbital, gr. ¼, is administered before each meal. Nitroglycerine and sodium nitrite may be tried. For the severe attacks, morphine and its derivatives may be required. However, if the attacks become frequent and the patient learns that relief follows these hypodermic injections, morphine addiction may result.

In some cases, despite conservative therapy, pain, weight loss and the incapacity to work persist. These patients require surgery. Numerous procedures have been advocated, and their great variety is an index of the different opinions underlying the pathologic physiology of this disease. Some surgeons have attacked the problem via the biliary system. Others have approached the pancreas directly, while a few have concentrated their efforts on the relief of pain by sectioning the sympathetic and parasympathetic nerve supply to the pancreas. The operative diagnosis of chronic pancreatitis in its incipiency is not an easy one. The interpretation of pancreatic pathology by palpation is open to great diagnostic error. The diagnosis of pancreatic disease in many instances can be made only by the microscopic examination of a specimen removed by biopsy. This can usually be done in chronic pancreatitis without fear of inducing either an acute pancreatitis or a pancreatic fistula.

As has been previously mentioned, the reflux of bile into the pancreatic duct is undoubtedly responsible for many cases of acute and chronic pancreatitis. Very often, following cholecystectomy in which the common bile duct is dilated, or is the site of stone formation, or occasionally following exploratory choledochostomy, operative or subsequent cholangiograms will reveal the presence of the pancreatic duct. However, it must be remembered that the roentgenologic demonstration of the pancreatic duct does not necessarily predicate a subsequent pancreatitis. Endocholedochal sphincterotomy in cases of intractable biliary dyskinesia has been previously demonstrated by Colp[22] to be effective in the relief of symptoms and to be unaccompanied by untoward effects. In 1945, an attempt was made to eliminate biliary reflux in a case of suspected pancreatitis by division of the ampullary muscle with the sphincterotomy.[23] Postoperative cholangiograms still resulted in visualization of the pancreatic duct. Despite the fact that a common channel persisted, this patient has experienced no further symptoms.

Recently a series of cases of chronic relapsing pancreatitis, in which biliary reflux played a major role, has been reported by Doubilet and Mulholland[24] in which endocholedochal and transduodenal sphincterotomy has been productive of excellent results. They, too, have had the experience of failure to divide the ampullary muscle via the common bile duct. Certainly, in these cases of definite chronic pancreatitis, in which the pancreatic portion of the common bile duct is apt to be narrowed, it might be more effective to perform routinely a transduodenal sphincterotomy.

In certain selected cases of severe chronic relapsing pancreatitis, the gland has been removed either completely or in part. Some good results have been obtained by this method, but the operation is a formidable one, accompanied by a high mortality, and the results are not always successful.[25] Pancreolithotomy has also been performed in other cases.[26] Sympathectomy plus cholecystogastrostomy, or choledochoduodenostomy was advocated by Mallet-Guy and his co-workers[27] in 1945. Nine cases in which previous operations on the biliary tract or the pancreas had been unsuccessful, were subjected to this procedure, the purpose being to relieve pain and diminish pancreatic secretion. Direct approach to the pancreas was not feasible because that organ was markedly edematous, hyperemic and adherent to contiguous structures, especially the superior mesenteric vein. Eight of the nine patients obtained considerable relief following operation.

DeTakats and Walter[28] performed splanchnic nerve section in a case of chronic pancreatitis and their patient was reported to have obtained considerable relief. Rienhoff and Baker[26] subjected a patient suffering from chronic pancreatitis to sympathectomy and vagotomy. A previous partial pancreatectomy and removal of stones had been performed without relief. Following sympathectomy and vagotomy, the pain was relieved, a gain of 60 pounds followed and morphine was no longer required. The success of this operation was ascribed to severance of afferent fibers in both the sympathetic and para-

sympathetic pain pathways, and to a diminution in pancreatic juice, caused by interference with the nervous mechanism of pancreatic secretion.

Subtotal gastrectomy was first performed by Colp[29] in 1947 in a case of chronic relapsing pancreatitis of 13 years duration. This case has been described previously, but a short summary is included in this report. Stimulated by the relief of symptoms in the first case, the same procedure was instituted in two additional cases of chronic relapsing pancreatitis. In both of these, a complementary vagotomy was performed. It is interesting to note that one of these cases had had a previous endocholedochal sphincterotomy, without relief of symptoms.

The rationale of subtotal gastrectomy in these cases has a fundamental physiologic basis. Secretin, which is formed by the action of hydrochloric acid, food, alcohol and certain drugs on the duodenal mucosa, is carried through the blood stream to the pancreas. The actual volume and bicarbonate content of the pancreatic juice is dependent on the degree of the secretin stimulus. When a subtotal gastrectomy of the Bilroth 2 type is performed, the production of hydrochloric acid is lessened by the elimination of the hormonal phase of gastric secretion, and the amount of acid is further neutralized by the regurgitation of the alkaline contents of the duodenum through the gastroenteric stoma. It is highly improbable that any acid chyme ever reaches the vicinity of the duodenum in the presence of a properly functioning gastroenteric stoma. As a result, secretin formation is diminished due to the diversion of the acid chyme; hence the lessened volume of pancreatic juice does not distend the pancreatic ducts which may be already narrowed by the pathologic changes incident to chronic relapsing pancreatitis. Pain is thereby relieved. The lessened amount of pancreatic secretion supplemented by the enzymes of the succus entericus, is apparently adequate for digestion.

The exact function of the vagus in pancreatic secretion is debatable, since both inhibitory and excitatory fibers in its pancreatic branches have been reported, but it has been shown by Babkin[30] and others that stimulation of the vagus produces a thick viscid flow of pancreatic juice rich in enzymes. Thomas[31] stated that cutting the vagus nerve in dogs has surprisingly little effect on pancreatic function, and concludes that there is more to the innervation of the pancreas than is comprised in the autonomic and parasympathetic fibers. However, division of the vagi to the stomach eliminates the psychic phase of gastric secretion and the resultant lowered acidity may account for some of the beneficial effects which have followed vagotomy for pancreatitis.

In the series of 29 cases of chronic relapsing pancreatitis reported by Comfort, Gambill and Baggenstoss,[1] two patients were subjected to partial gastrectomy. These operations were done primarily for the relief of ulcer symptoms. One patient, a 32-year-old alcoholic had suffered from chronic pancreatitis for two years before experiencing several gastric hemorrhages. At operation, no gastric pathology was found, but because of the hemorrhages, partial gastrectomy was done. This patient was reported as unimproved.

Another patient, a 31-year-old brewery worker, known to have chronic pancreatitis for three years, showed radiographic evidence of a duodenal ulcer. Exploration revealed some thickening of the upper part of the pyloric sphincter muscle, but no ulcer. Partial gastrectomy was done and 11 months after operation, the patient was reported definitely improved.

Three patients admitted to the Mount Sinai Hospital suffering from chronic pancreatitis were subjected to subtotal gastrectomy, and in two a complementary vagotomy was added. The case histories are herewith submitted.

CASE REPORTS

Case 1.—(569703) C. V., a 45-year-old bartender, who had been accustomed to heavy drinking for many years, had been admitted to the Mount Sinai Hospital on 8 different occasions between 1941 and 1947. His presenting complaints on each admission had been upper abdominal pain of varying severity accompanied by nausea, vomiting and at times, shock. He had undergone one operation in 1943 for acute pancreatitis, at which time cholecystectomy and prolonged T-tube drainage were performed. The pancreas and the omentum showed numerous areas of fat necrosis, but the gallbladder contained no stones, although the gallbladder wall was chronically inflamed. He experienced no relief after his operation and his course was unremitting in that he suffered from severe pain, weakness, weight loss and diarrhea. Ultimately, pancreatic calcification, creatorrhea and steatorrhea were demonstrated.

In 1947, a gastric ulcer developed for which subtotal gastrectomy was performed. The results in terms of relief of pain, restoration of strength and disappearance of diarrhea, creatorrhea and steatorrhea were dramatic. At the present writing, 22 months after operation, this patient is free of pain and has gained 15 pounds. His diarrhea has disappeared and his stools have returned to normal. He is able to work steadily for the first time in 8 years.

Case 2.—(588344) S. S. was admitted to the Mount Sinai Hospital on November 17, 1947. This 52-year-old white married female had had 3 severe attacks of epigastric pain during the past 3 months which were diagnosed and treated as biliary colic. At the first attack in August, icterus was noted and in October after her third attack, she was again jaundiced. For the past 5 years, she had been treated at intervals for duodenal ulcer. Recent roentgenograms of the gallbladder had shown the presence of stones.

At operation on November 18, 1947, under spinal anesthesia, the gallbladder was found to contain several stones, and the common bile duct was dilated. Several small stones were removed from the choledochus, and an endocholedochal sphincterotomy was performed to paralyze the sphincter. The common duct was drained. No significant changes were found on palpating the pancreas. Her postoperative course was uneventful.

On December 29, 1947, she was re-admitted with the signs of a right subphrenic abscess which had developed subsequent to her discharge from the hospital. After a course of penicillin therapy, she improved and operation was deemed unnecessary. She remained well until January 22, 1948, when she experienced a severe attack of epigastric pain radiating to the back associated with chills and fever. On conservative treatment, the temperature dropped to normal, and symptoms were relieved.

She continued to have mild attacks of epigastric pain simulating biliary colic, and she returned to the hospital on April 10, 1948. Because of the distribution of pain to the left, and in view of persistence of symptoms, despite sphincterotomy, it was felt that the patient was having attacks of subacute pancreatitis. Plain films of the abdomen revealed no

calculi. There was no glycosuria or hyperglycemia, and the stools were grossly normal. Blood amylase varied between 30 and 80 mg. of sugar per 100 cc. Alkaline phosphatase was 9 K.A. units. Cephalin flocculation was 2 plus.

The patient was re-explored under spinal anesthesia on April 15, 1948. At operation, the pancreas was found to be the site of a diffuse acute and chronic inflammatory process. The organ was very firm and enlarged. No calculi were felt. A biopsy of the pancreas was taken (Fig. 1). The common bile duct was not dilated and no calculi were palpable.

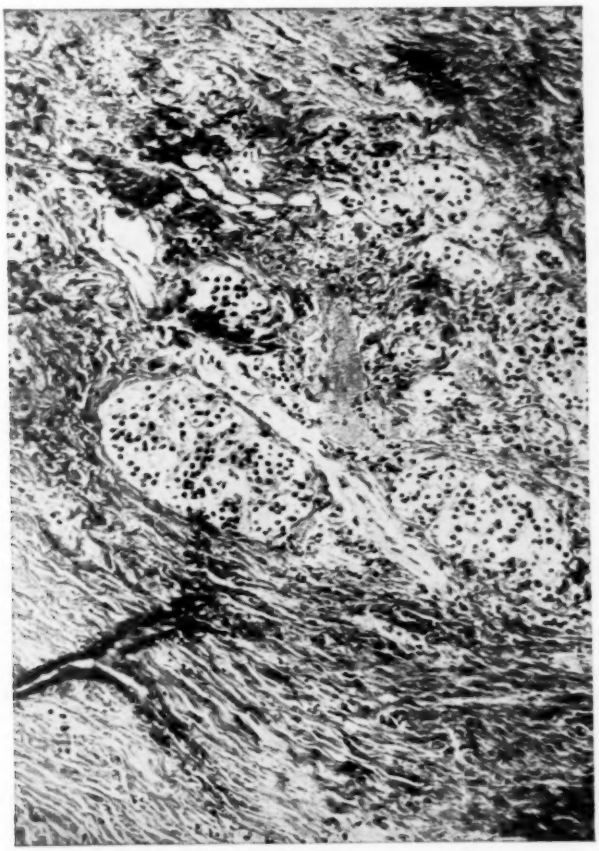

FIG. 1.—(Case 2) Biopsy of pancreas showing marked fibrosis and some residual inflammation indicating chronic and subacute pancreatitis.

A subtotal gastrectomy of the Hofmeister type with an antecolic terminolateral gastrojejunostomy and a complementary bilateral infradiaphragmatic vagotomy were performed. Biopsy of the pancreas was later reported as showing subacute and chronic pancreatitis.

The postoperative course was uneventful. She was seen in the follow-up clinic at intervals, and in July, 1949, 15 months after her operation, she reported that she had gained 5 pounds, was no longer experiencing any abdominal pain, and that she was well enough to carry on all her household duties. At this time, a secretin test of pancreatic function revealed normal volume and bicarbonate response and diminished enzyme concentration.

Case 3.—(586623) B. R., a 34-year-old handyman, was well until 1940, when he was admitted to the Mount Sinai Hospital with a 4-hour history of upper abdominal pain, nausea and vomiting. He admitted to being a heavy drinker. Physical findings indicated the possibility of a perforated peptic ulcer, and, accordingly, the patient was explored. The stomach and duodenum showed no evidence of an ulcer, but the gastro-hepatic omentum was markedly edematous and congested, and the operator's impression was that acute pancreatitis was present. The patient made an uneventful recovery.

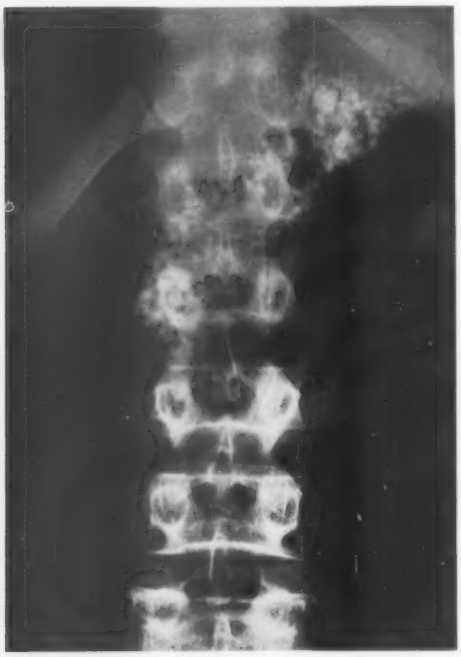

FIG. 2.—(Case 3) Plain film of abdomen showing extensive calcification in the region of the pancreas.

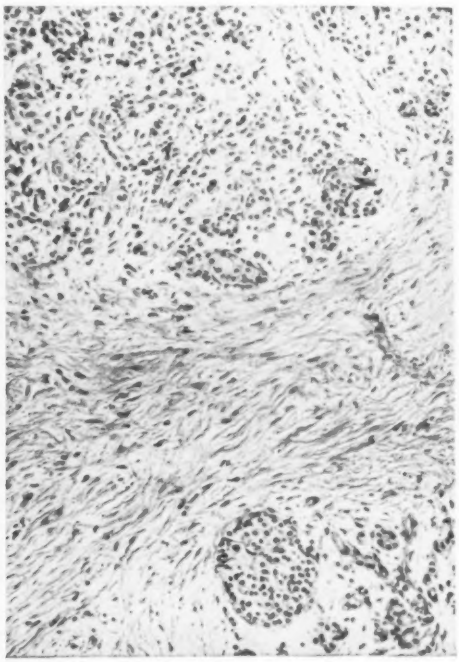

FIG. 3.—(Case 3) Biopsy of pancreas showing dense fibrotic replacement and some relatively uninvolved pancreatic tissue.

He was not seen again until 1947, when he reappeared in the Outpatient Department complaining of weakness, easy fatigability and diarrhea. He stated that he had been treated on the wards of another hospital on 2 occasions, and in the clinic of a second hospital at numerous other times for recurrent abdominal pain. No definite diagnosis had ever been made. He admitted no change in his drinking habits. His face was thin and drawn and his color somewhat yellowish. The abdomen was flat, and no enlarged viscera or other masses were felt. Flat plate of the abdomen revealed numerous calcific shadows in the upper abdomen in the region of the pancreas (Fig. 2). Examination of the stool disclosed considerable fat, and undigested muscle fibres. Urine and blood examinations showed no glycosuria or hyperglycemia. The secretin test for pancreatic function gave evidence of markedly diminished secretion. A diagnosis of chronic relapsing pancreatitis was made and medical therapy in the form of high protein, high carbohydrate diet supplemented by pancreatin, was instituted.

He returned to clinic on October 6, 1948, complaining of persistent upper abdominal pain, weakness, weight loss and diarrhea. Physical findings were essentially the same as on his last outpatient visit, plus the additional discovery of a flat, firm, oval-shaped mass

about 6 inches across and 3 inches long, deep in the epigastric region. Blood count revealed a hemoglobin of 10.4 Gm., white blood cells 10,900, 72 per cent polys, 22 per cent lymphs, and 6 per cent monocytes. Stool guaiac was negative. Considerable fat and undigested protein were seen on microscopic examination of the stool. Urine showed 2 per cent sugar. Blood sugar was 329 mg., urea nitrogen 8, total protein 6.4, amylase equal to 40 mg. glucose per 100 cc. Glucose tolerance test disclosed a hyperglycemic curve with the specimen at the end of 3 hours reported as 540 mg. of glucose per 100 cc. Pancreatic function studies demonstrated a volume of 69 cc. in a 2 hour period with bicarbonate concentration of 29 milliequivalents per liter, and amylase of 0.3 u/h, all evidence of markedly diminished pancreatic secretion.

Operation was performed under spinal anesthesia on October 18, 1948. The pancreas was stony hard and felt like a bag of stones. The stomach and duodenum were normal. Biopsy of the pancreas was taken. A subtotal gastrectomy of the Hofmeister type was performed with an antecolic terminolateral gastrojejunostomy with complementary bilateral infra-diaphragmatic vagotomy. The biopsy was reported as showing marked fibrosis and calcification (Fig. 3). The postoperative course was uneventful. He was discharged on November 10, very much improved. He had no pain and his diarrhea had lessened considerably. He was maintained on a 2500 caloric diet (260-140-100) with 30 units of Protamine Zinc insulin and 10 units of regular insulin daily.

He reported to the clinic at regular intervals following his discharge, up to February 2, 1949, at which time he was free of pain. He said that his wife had left him and that he had no relatives with whom he could take up residence. He felt that maintenance of his dietary and insulin regimen would be very difficult. He kept no further clinic appointment. Despite diligent search by the Social Service Department he could not be located and it was not until we received a report from another hospital that we learned of his death six weeks after his last visit to us.

Information was provided to the effect that he had been admitted to this hospital three weeks before his death in a state of severe weakness and emaciation. A diagnosis of diabetes mellitus secondary to chronic pancreatitis was established and he was treated for diabetic acidosis and occasional insulin hypoglycemia to no avail. He expired in deep coma on March 20, 1949.

At autopsy, the pancreas was found to be extremely firm and fibrotic. Lodged in the duct of Wirsung from its termination in the ampulla of Vater and extending along the duct to the tail of the pancreas were innumerable small white chalky stones averaging 5 mm. in diameter. The duct itself was markedly dilated. The parenchyma of the pancreas was filled with many smaller stones. The pancreatic and common bile ducts entered separately into the duodenum and did not have a common connecting channel.

Other gross findings were a high subtotal gastrectomy and a functioning anterior gastrojejunostomy, fatty infiltration of the liver and a severe bilateral septic lobular pneumonia. Microscopic examination of the pancreas showed almost complete replacement of the pancreas by fibrous tissue with scattered islets of Langerhans remaining.

DISCUSSION

These three cases are illustrative of many of the features of chronic relapsing pancreatitis. Alcoholism was the contributing etiologic factor in two, biliary tract disease was present in two. Two patients had undergone previous operations on the biliary tract, and in one of these an endocholedochal sphincterotomy had been performed. All patients presented the important disabling features of pancreatitis, that is, pain, diarrhea and dyspepsia, which were sufficiently distressing to prevent gainful employment. The diagnosis of chronic pancreatitis was made by biopsy taken from the pancreas in each

case. Following subtotal gastrectomy, two were relieved of their symptoms. The third patient obtained relief from pain but experienced marked aggravation of his diabetes, resulting in death in diabetic coma.

This latter case corroborates the concept that structural damage to the pancreas is permanent. In most cases, however, if the diabetes is adequately treated, such serious aftermath should not be expected to ensue.

Further damage to the pancreas may be prevented by minimizing excessive periodic stimulation of the secretin mechanism. Heightened secretory activity may be accompanied by obstruction of the pancreatic ducts. The latter may be caused either by edema of the duodenal mucous membrane or regurgitation of the succus entericus, or biliary reflux, or metaplasia within the ducts, or constriction of the ducts by calcification and periductal fibrosis. This obstruction will lead to a marked increase of pressure within the ducts which may produce either a diffusion of the enzyme into the parenchyma or a rupture of the radicles with the production of acute pancreatitis. Repeated attacks of this nature lead to chronic relapsing pancreatitis. Although structural damage is permanent, the pathologic cycle which will eventually lead to transformation of the pancreas into a calcified functionless mass and the disintegration of the patient into a chronic invalid, is apparently arrested by subtotal gastrectomy. Vagotomy may act to further minimize pancreatic secretion and implement the effect of subtotal gastrectomy.

As methods of diagnosis improve, and chronic relapsing pancreatitis is recognized more often as a clinical entity, fewer patients will be relegated to the psychoneurotic group. The medical therapy which has been outlined might be of value in the mild cases, but the incapacitated patient will require surgery. Subtotal gastrectomy offers a rational physiologic approach and has produced excellent results in two cases and relief of pain in a third. Before definite conclusions can be drawn as to the ultimate value of this procedure in chronic pancreatitis, a longer period of follow-up is required, and additional patients in whom this procedure may be done by others, should be studied carefully.

SUMMARY

The etiology, pathology, and clinical features of chronic relapsing pancreatitis are reviewed. A tenable theory based on disturbance of the secretin mechanism of pancreatic secretion is presented.

The medical measures and surgical procedures advocated for the control of the symptomatology are outlined. The rationale of subtotal gastrectomy in the treatment of chronic pancreatitis is discussed, and the histories of two cases in which this procedure was successful, are detailed. A third case in which severe diabetes supervened is described.

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INTESTINAL OBSTRUCTION

THE PROTECTIVE ACTION OF SULFASUXIDINE AND SULFATHALIDINE TO THE ILEUM FOLLOWING VASCULAR DAMAGE*

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INTRODUCTION

INTESTINAL OBSTRUCTION is a complex entity made up of numerous variable factors which cannot be separated and isolated for definitive experimental study. Two important factors are the blood supply of the bowel and the intraluminal bacterial flora. The importance of the former under altered conditions of the latter has been the object of considerable investigative work. Poth and associates[8-13] have shown in numerous publications that the bacterial flora of the intestine can be changed appreciably by the oral administration of sulfasuxidine and sulfathalidine.

While working on the factor of blood supply, Scott and Wangensteen,[17] Foster and Hausler,[3] and Murphy and Vincent[6] found that obstruction of the mesenteric veins produced death in dogs more rapidly and more frequently than other types of mesenteric vascular occlusion. Recently, Sarnoff and Poth[16] and Sarnoff and Fine[15] found approximately 90 per cent of dogs weighing ten kilograms would die within 48 hours from simple interruption of the mesenteric veins to a 50 cm. segment of terminal ileum. Death was consistently due to peritonitis. In the experiments of Sarnoff and Poth,[16] all control animals had large perforations in the loop of bowel under study, while Sarnoff and Fine[15] observed 75 per cent gross perforations.

The same observers also found that by administering sulfasuxidine or sulfathalidine orally for several days before venous ligation only 25 to 30 per cent of the animals died within 48 hours and 70 to 75 per cent survived indefinitely. This difference of survival is significant.

If sulfa drugs were given at the time of operation or immediately after, protection was afforded to a smaller number of animals. Sarnoff and Fine injected, by means of a needle and syringe, 1 Gm. per Kg. of body weight of sulfasuxidine into the lumen of the proximal bowel at the time of operation. In this group 34 per cent of the animals survived. They gave another group of dogs parenteral sodium sulfathiazole for two days after the operation. This procedure resulted in the survival of four out of eight animals. The number

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of animals is small and the differences observed in the survival rate may well be insignificant.

Subsequently, Blain[1] demonstrated that parenteral penicillin would protect, for a limited period of time, dogs which had been subjected to mesenteric venous ligation. The experiment was different in that the terminal ileum was divided and the ends inverted so as to produce a complete obstruction. The veins in the proximal 60 cm. segment were then ligated. Death overcame all control animals in less than 36 hours, even though they were treated for shock, hemorrhage, and fluid loss. Perforation was "often" observed in the controls and all showed massive bacterial invasion of the infarcted walls of intestine. The percentage of perforations in treated animals is not reported. On the other hand, most of the animals given massive doses of penicillin survived three to four times as long, and some were cured after resecting the infarcted bowel 72 hours following ligation. The important role of bacterial infection in cases of intestinal obstruction was re-emphasized.

The visible changes in a loop of bowel after venous ligation are very interesting. The normal color is replaced by cyanosis, which progresses to a deep reddish purple within 20 to 30 minutes. The involved segment is sharply demarcated from the normal. Engorgement of the bowel wall and the mesenteric veins continues until the pressure within them equals the arterial capillary blood pressure. Shortly thereafter arterial pulsations cease. If the infarcted segment is incised there is practically no bleeding, indicating that early thrombosis has occurred. Histologic sections of the bowel taken at different intervals postoperatively confirm these observations. There is widespread thrombosis in veins of untreated animals, while thrombosis in the veins of surviving treated dogs is minimal.

In a further investigation of this subject, the influence of ligating the arteries to a corresponding segment of ileum, as well as that of the simultaneous ligation of arteries and veins, is studied and reported in this communication.

EXPERIMENTAL PROCEDURE

In the experiment, healthy mongrel dogs were divided into two groups. One, the controls, received only horse meat for ten to 16 days before operation; the other, treated animals, received 1 Gm. per Kg. of body weight per day of sulfasuxidine, or ½ Gm. per Kg. per day of sulfathalidine, mixed with the horse meat given every four hours for the same length of time. The dogs were in a weight range of seven to 12 Kg., most of them weighing approximately 10 Kg. After operation, the animals were offered water but no food for the first two days, then they were fed for ten days in the same manner as before operation. While on a diet of horse meat, the control dogs often developed a diarrhea with very foul stools. However, the dogs receiving horse meat plus sulfasuxidine rarely developed diarrhea and frequently would go seven to ten days without a bowel movement. Their feces were soft and devoid of the unpleasant odor always found in those not receiving the drug.

The operative procedure, done under ether anesthesia and aseptic technic, is briefly as follows. The peritoneal cavity is entered and the terminal ileum located. A segment of ileum 50 cm. in length is selected 10 cm. proximal to the termination of the antimesenteric artery (Fig. 1) so as to avoid collateral circulation from this vessel. Occasionally, when a dog weighed less than 10 Kg., a length of 5 cm. of bowel per Kg. of body weight was similarly isolated. At either end of the segments the mesentery is divided down to its root and includes the careful ligation of the arteries and veins running parallel to the bowel in its mesenteric border. Near the base of the mesentery, the arteries

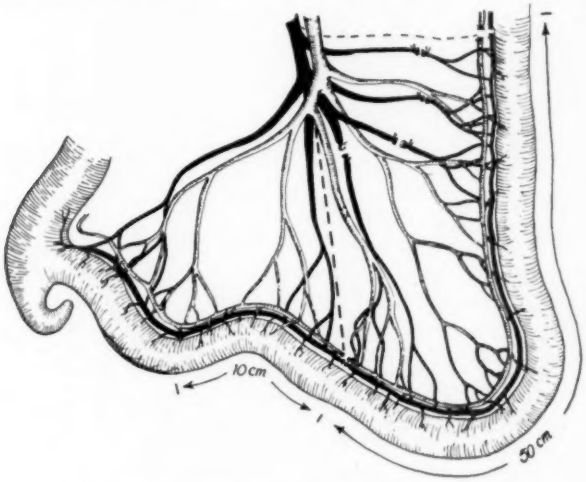


FIG. 1.—A schematic representation of the segment of ileum 50 cm. long and located 10 cm. proximal to the termination of the antimesenteric artery. In this instance the division and ligation of the veins is indicated.

or arteries and veins are isolated. If arteries alone are divided and ligated, care is taken to avoid injury to the veins which are left intact. The changes which occur after such a procedure are quite striking. Immediately upon interruption of the arterial blood supply, the vessels collapse distal to the ligature. The bowel undergoes violent peristaltic and spastic contractions, causing it to become nodular, blanched, and one-half its original length. Cyanosis develops within a few minutes and the veins become distended with dark blood. If arteries and veins are ligated simultaneously, there is a similar immediate reaction, but the vessels and bowel become engorged and cyanotic much more rapidly.

Among control animals, there is a very high mortality during the first three days after operation. These animals die of a massive acute fulminating peritonitis. The peritoneal cavity is distended with bloody purulent fluid. All peritoneal surfaces are intensely inflamed. The limits of the ligated segments are sharply demarcated and deep bluish-red in color. The midportion of the segment is autolysed, sometimes completely destroyed or containing very large perforations with only portions of the serosa and the muscularis

remaining attached to the mesentery (Fig. 2). In the mesentery there is dilatation and engorgement of smaller vessels with thrombosis and extravasation of blood along the larger ones. On the surface, and sometimes between the leaves of the mesentery, there is a fibrinous exudate. In the majority of

FIG. 2

FIG. 3

FIG. 2.—(Experiment C-25). This animal had not received sulfasuxidine before arterial interruption. Death occurred 48 hours postoperatively with nearly complete autolysis of the segment. The chain shown is 50 cm. long and represents the initial length of the segment of ileum which has become shortened to approximately half its length at time of ligation. This extent of destruction is the usual result in the control animals.

FIG. 3.—(Experiment S-74). This animal received sulfasuxidine before the simultaneous ligation of the arteries and veins to a 50 cm. segment of ileum. The animal was alert and active on the third postoperative day when sacrificed. There was some discoloration of the segment which had become shortened to 20 cm. There were no perforations, no peritonitis. This animal would have survived. The mesentery is not yet shortened.

cases, the intestines are massed together and enveloped by the omentum. When there is almost complete destruction of the bowel, however, there may be no adhesions.

Among the four control dogs which survived the immediate postoperative period, one died of intestinal obstruction from adhesions and volvulus after ten days. Another died from an undetermined cause at two weeks; the peri-

toneal cavity was not remarkable. The other two were sacrificed at different intervals. This phenomenon of late obstruction was observed in only three of the treated animals, although the number of animals surviving the acute phase was much greater.

When dogs are given sulfasuxidine or sulfathalidine preoperatively and are subjected to the same operation, there is a comparatively low mortality and most of them survive and appear normal. In order to follow the immediate recovery and eventual healing after operation, dogs were sacrificed for colored still and motion pictures at daily intervals for seven days, then at ten, 15, 20, 30, 50, 75, and 100 days, six months, and nine months.

Although there was considerable variation in the intensity of the inflammatory reaction among the treated survivors, the protective mechanism was in general the same. There was no free fluid found in the peritoneal cavity after the first week; some animals had none even on the second and third days. When present it was small in volume and serosanguineous in character.

The involved segment was frequently folded upon itself with the adjacent loops of bowel coiled in a mass closely enveloped by the omentum. There were numerous fibrinous adhesions between loops of bowel as well as with the omentum. These adhesions vascularized early and bled freely when separated five to ten days postoperatively. During the first week, the inflammatory reaction was usually conspicuous. In some instances the segment was sharply demarcated from the normal intestine at either end (Fig. 3); in others there was little discoloration except for small areas in the center of the loop. In the mesentery, there was dilatation and engorgement of blood vessels with extravasation and exudation along the larger mesenteric vascular trunks as well as on the surface. Thrombosis was not conspicuous. From the period immediately after ligation of the vessels, the loop of bowel was always found to be shortened ½ to ⅓ its original length. After two to four weeks the inflammatory reaction had largely subsided and the bowel was normal in color, although some thickening of the bowel wall persisted. After several weeks or months, there was no demonstrable scar contracture of the bowel wall, and in only one case, 11 months postoperatively, was an annular fibrosis found which reduced the size of the lumen. In this case it was not significant. There was no obstruction. The dog had grown and doubled in weight since operation.

Concomitant with contraction of the length of the bowel there is a shortening of the mesentery. The process continues along with thickening and fibroplastic proliferation around the severed ends of the vessels, and by two weeks to one month it will have shortened one-half to one-third its original length (Fig. 4). Later, when the scar tissue contracts, there is further decrease in length so that the intestine may be resting almost on the mesenteric lymph nodes.

Retractile mesenteritis was first produced experimentally by Jura[5] in 1924 by injecting intestinal bacteria into the mesentery of the ileum. Stropeni[18] (1933) produced the condition by ligating or injecting the mesenteric veins but not following ligation of the arteries. Reichert, Gerbode and Halford[14]

(1939) concluded that retractile mesenteritis could be produced by ligation of all vessels in the mesentery, by ligation of the lymphatics alone, and by irritation or trauma of the leaves of the mesentery. In the ligations of the vessels to the long segments of ileum as practiced in this study, shortening of the mesentery as well as of the bowel itself occurred regularly, regardless of whether arteries, veins, or arteries and veins were ligated. The factor of bacterial infiltration of the bowel wall and tissues of the mesentery was undoubtedly always present and was likely the most important factor in these studies. Dilatation of lymphatics was not observed, and, in all probability, the

FIG. 4.—(Experiment S-60). Arterial ligation after sulfasuxidine administration. The animal was sacrificed 75 days postoperatively. Normal peristalsis had been restored. The segment is contracted to 1/3 its original length, but its diameter is not reduced. The corresponding mesentery is strikingly shortened. Adhesions were minimal.

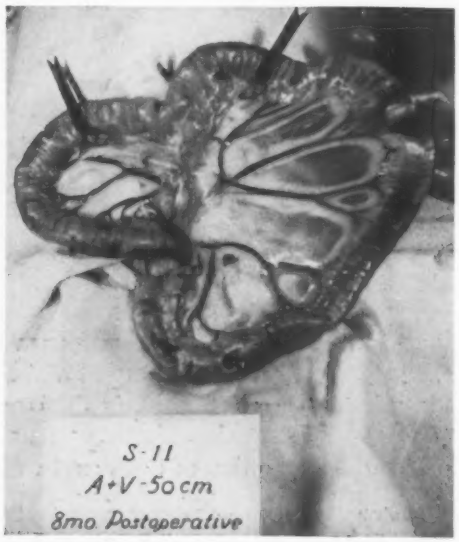


FIG. 5.—(Experiment S-11). Simultaneous ligation of arteries and veins after sulfasuxidine administration. The animal was sacrificed eight months postoperatively. This shows essentially the same findings as S-60 in Figure 4. The arrows indicate the ends of the segment.

lymphatics were not completely interrupted. The characteristic thickening and fibrosis of the wall of the bowel seen in regional enteritis was not produced in these experiments.

If the mesentery is examined closely after the acute phase, small blood vessels can be seen bridging the gap around the severed ends of the large mesenteric arteries and veins, so that through these small collaterals the original vessels re-establish function. This finding is demonstrated in Figure 6. Roentgenographic examination of specimens injected with radiopaque material demonstrates the manner in which revascularization occurs (Figs. 6 and 7).

TABLE I.—*Tabulation of Results of the Division of the Arteries to Segments of Distal Ileum of a Group of Control Animals.*

Animal No.	Weight in Kg.	Length of Segment	Lived	Comments
1	10	50 cm	14 hrs.	Died. Large perforation with massive peritonitis.
6	10	50 cm	30 hrs.	Died. Large perforation with much free fluid in peritoneal cavity. Diffuse crepitus in viscera and walls.
7	9	25 cm	48 hrs.	Sacrificed. Was very ill. Large walled off perforation; much free fluid in cavity.
10	10	40 cm	50 hrs.	Sacrificed. Large perforation of gut. Would have died shortly. Massive peritonitis; much free fluid.
11	11	35 cm	3 days	Sacrificed. Large perforation of gut, walled off, much free fluid. Would have died.
13	10.5	25 cm	1 week	Sacrificed. Was doing well. Reaction subsiding, would have recovered.
16	18.5	50 cm	36 hrs.	Died. No perforation; much free fluid, massive peritonitis.
18	11	50 cm	4 days	Died. Large perforation. Much free fluid; massive peritonitis.
20	10	50 cm	3 days	Died. Much free fluid; large perforation; massive peritonitis.
22	13.5	50 cm	48 hrs.	Died. Much free fluid; autolysis with large perforation; massive peritonitis.
24	9	40 cm	36 hrs.	Died. Much free fluid; autolysis with large perforation; massive peritonitis. Photographed.
23	11	50 cm	10 hrs.	Died. Much free fluid; complete obstruction adhesions and volvulus. No perforation.

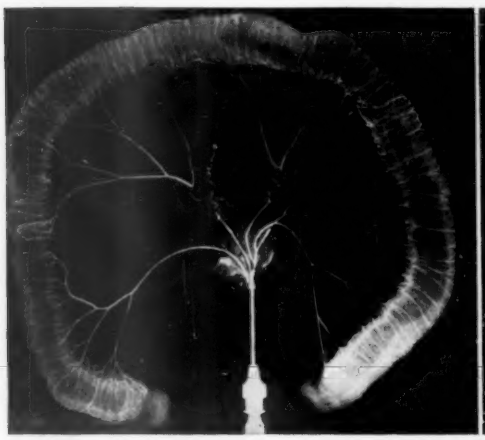


FIG. 6

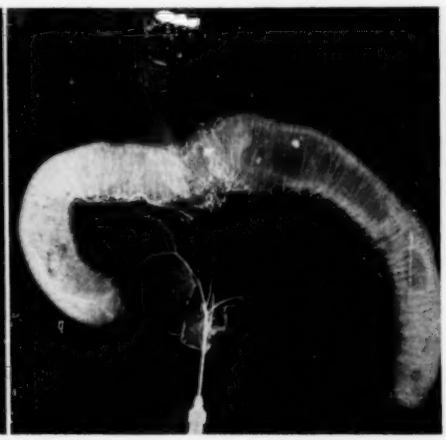


FIG. 7

FIG. 6.—(Experiment S-29). This dog was sacrificed 5½ months after the simultaneous ligation of both arteries and veins following sulfasuxidine administration, and injected with BiOCl suspension (Poth[7]). Roentgen ray film shows development of collaterals between ends of severed arteries, across the mesentery from an adjoining artery, and a definite increase of vascularity in the wall of the bowel at either end of the segment. This latter is the only available circulation immediately following operation, and serves to sustain the bowel for a considerable period until other vessels can become established.

FIG. 7.—(Experiment S-24). This dog was sacrificed eight months after the simultaneous ligation of arteries and veins to a 50 cm. segment of distal ileum following sulfasuxidine administration and then injected with BiOCl suspension. Roentgenogram shows the collaterals, especially in the wall of the bowel and through an omental adhesion. This segment is obviously greatly shortened.

During the first several days after operation the mucosal layer is usually edematous and hemorrhagic. However, within one to two weeks, it regains its normal color and consistency, and the folds resume their usual pattern without evidence of deformity by scar formation.

As mentioned before, there were only three intestinal obstructions in the animals receiving drug, even though there were always numerous adhesions and kinks in the bowel. With the eventual establishment of adequate collateral circulation through the mesentery and through the bridges around the severed

TABLE II.—*Tabulation of Results of the Simultaneous Interruption of Both Arteries and Veins to Segments of Distal Ileum of a Group of Control Animals. Animal 3 Had Only the Vein Divided.*

Animal No.	Weight in Kg.	Length of Segment	Lived	Comments
2	9.5	50 cm	36 hrs.	Sacrificed. Autolysis of segment with perforation and massive peritonitis.
4	10	50 cm	30 hrs.	Sacrificed. Necrosis but no gross perforation. Crepitus extensive in peritoneal cavity and abdominal wall.
5	6.5	50 cm	30 hrs.	Sacrificed. Large perforation with massive peritonitis.
8	10	25 cm	50 hrs.	Sacrificed. Might have lived. No perforation, little free fluid. Mass well walled off.
9	14	30 cm	36 hrs.	Sacrificed. Very large dog. Autolysis of segment. Massive peritonitis with crepitus.
12	8	40 cm	36 hrs.	Sacrificed. Much free fluid; large perforation walled off.
14	11	25 cm	2 weeks	Sacrificed. Was doing well. Peritoneum clean, healing well.
15	16	50 cm	7.5 mo.	Sacrificed for photograph. Only control dog to live. Well healed; omentum adherent to bowel.
17	8	40 cm	2 weeks	Died. Cause unknown. Peritoneum clean—some adhesions, no obstruction.
19	9	50 cm	48 hrs.	Sacrificed. Much free fluid; massive peritonitis; segment very dark and soft; no perforation.
21	10	50 cm	3 days	Sacrificed. Much free fluid; autolysis with large perforation; massive peritonitis.
25	10	50 cm	36 hrs.	Sacrificed. Much free fluid; autolysis with large perforation and massive peritonitis.
3	11	50 cm	18 hrs.	Sacrificed. Much free fluid; autolysis with large perforation and massive peritonitis.

ends of the parallel vessels many of the adhesions resolve, and the number of adhesions persisting after six months was much fewer than within a month of the procedure. The omentum usually remains attached to the segment, but occasionally the loop lies free in the peritoneal cavity.

The results of these experiments are summarized in Tables I, II, III, and IV.

The difference in survival rates between control and treated animals is readily presented in graphic form, (Figs. 8, 9, 10 and 11). In the control series the mortality rate during the first four days ranged from 80 to 100 per cent. Among the treated animals 30 to 35 per cent died within this four-day period with a final survival rate of approximately 50 per cent.

DISCUSSION

The rôle played by the blood supply and the importance of its preservation in the final outcome of obstruction of the bowel are again emphasized in these

FIG. 8

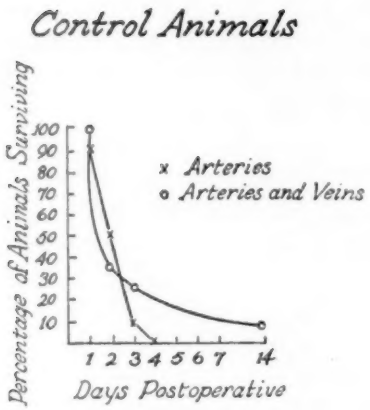
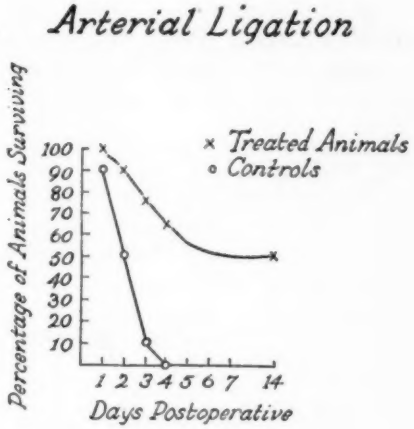
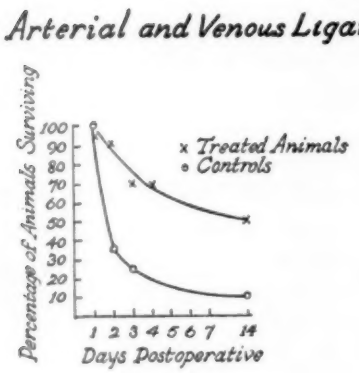


FIG. 9





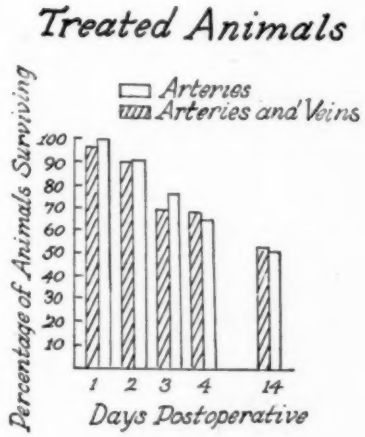


FIG. 10

FIG. 11

FIG. 8.—A plot of survival of control animals following the ligation of arteries and arteries and veins to 50 cm. segments of distal ileum. Within the limits of the experiment, they are identical.

FIG. 9.—A plot of survival of control and treated animals following interruption of arteries to 50 cm. segments of distal ileum.

FIG. 10.—A plot of survival of control and treated animals following the simultaneous division of both arteries and veins to 50 cm. segments of distal ileum.

FIG. 11.—A plot of survival of treated animals following the ligation of arteries in the one instance and the simultaneous interruption of arteries and veins in the other to 50 cm. segments of distal ileum. Within the limits of error of these experiments there is no difference.

studies. It would appear that the value of sulfasuxidine or sulfathalidine resides in their ability to alter the bacterial flora in the lumen of the bowel and thereby reduce the bacterial invasion and impregnation of the tissues of the bowel by toxic substances, which in turn cause thrombosis of the blood

TABLE III.—*Summation of Results Following the Division of the Arteries to 50 cm. Segments of Distal Ileum of 35 Dogs Which Had Received Oral Sulfasuxidine or Sulfathalidine Preoperatively and Postoperatively.**

Animals living 5 days or less		17
Died	2	
Sacrificed†	15	
Peritonitis	12	
Perforation of ileal loop	8	
Animals living 7 days to 9 months		18
Died	0	
Sacrificed	18	
Peritonitis	0	
Perforations of ileal loop	0	
Total		35

* The detailed tabulation of these data is being published in *Texas Reports on Biology and Medicine.*
† Ten of these 15 animals had peritonitis with perforation of the ileal loop in 8 instances.

vessels in the bowel wall, especially the terminal arterioles and capillaries. The preservation of the blood supply by preventing thrombosis and the reduction of toxic bacterial products are sufficient to protect the tissues of the bowel from necrosis and perforation.

The preservation of adequate blood supply is, however, dependent upon factors other than prevention of vascular thrombosis. In addition it is influ-

TABLE IV.—*Summation of Results Following the Division of Both Arteries and Veins to 50 cm. Segments of Distal Ileum of 37 Dogs Which Had Received Oral Sulfasuxidine or Sulfathalidine Preoperatively and Postoperatively.**

Animals living 5 days or less		16
Died	0	
Sacrificed	16	
Peritonitis	14	
Perforation of ileal loop	9	
Animals living 6 days to 9 months		21
Died	0	
Sacrificed	21	
Peritonitis	0	
Perforation of ileal loop	0	
Total		37

* The detailed tabulation of these data is being published in *Texas Reports on Biology and Medicine.*

enced by maintenance of the circulating blood volume. When the survival rates at 48 hours following ligation of veins, arteries, and arteries and veins simultaneously are analyzed, it is found that, both among the control experiments and those animals receiving sulfonamide treatment, the mortality is greatest among those where only the veins are divided.

Mortality Rates Within 48 Hours of Operation

	Venous Ligation	Arterial Ligation	Arterial and Venous Ligation
Control animals — Per cent mortality.....	95	50	64
Treated animals — Per cent mortality.....	27	9	9

Following venous ligation death usually occurs within the first 48 hour postoperative period. There is rapid loss of blood into the wall and lumen of the bowel when the veins alone are interrupted, reducing the circulating blood volume, inducing a greater degree of shock, and augmenting the mortality during the early postoperative period. This is true, although eventually the survival rate of the treated animals is greater following venous ligation than after arterial or simultaneous arterial and venous ligation.

A comparison of the results following arterial ligation alone with the simultaneous division of both arteries and veins to segments of ileum fails to show the beneficial effect of accompanying the arterial interruption with venous ligation as observed by Brooks and Martin[2] and Holman[4] in prevention of gangrene of the leg of the dog following ligation of the iliac artery. The situation here might, however, be different in that bacterial invasion of the wall of the bowel with liberation of toxic substances may be the predominating factor overshadowing all others, while infection would be insignificant following interruption of the iliac artery.

Sulfasuxidine and sulfathalidine have been given in cases of mesenteric infarction in the hope of preventing progression of the intravascular clot or to protect the bowel should there be further mesenteric embolism. Our limited experience with this therapeutic application prevents any reasonable evaluation of the measure.

The influence of the intestinal flora on bowel necrosis and perforation has been demonstrated, and it has been shown that this effect can be significantly reduced by the antibacterial action of sulfasuxidine and sulfathalidine.

SUMMARY

The importance of the bacterial flora as a factor in bowel necrosis in the presence of vascular damage is studied.

The bacterial flora is altered and attenuated by the administration of sulfasuxidine and sulfathalidine.

Vascular damage is inflicted by division of arteries, veins, and arteries and veins simultaneously to segments of distal ileum and the results with and without sulfonamide therapy are studied.

The pathologic alterations and the mode of repair is described.

It is concluded that the bacterial flora is an important factor in bowel necrosis in intestinal obstruction.

Sulfasuxidine and sulfathalidine have a distinct favorable effect to promote repair of damaged intestinal tissues.

The administration of sulfasuxidine or sulfathalidine is proposed when intestinal infarction is suspected and whenever intestinal surgery is contemplated.

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THE ESOPHAGEAL ARTERIES

THEIR CONFIGURATIONAL ANATOMY AND VARIATIONS IN RELATION TO SURGERY*

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INTRODUCTION

THE ESOPHAGEAL ARTERIES have in the past two or three decades attained a surgical significance unforeseen to the classical anatomists. The conventional extremely brief descriptions of the circulation of the esophagus available in standard anatomic texts are based on the relatively few investigations conducted from the sixteenth through the nineteenth centuries. Few definitive studies of the arterial distribution of the esophagus, none of a scope commensurate with current surgery, or in the English language, have appeared in the past 75 years.

The usual anatomic test,[1-14, 58-79] treatise, or atlas description in entirety is somewhat as follows: "The arterial supply of the esophagus is derived from the inferior thyroid, the esophageal branches of the aorta, the intercostals, the inferior phrenic, and the left gastric arteries." Further informative detail is exceptional and meager at best. Almost no statement can be found concerning configurations and variational morphology.

Since Torek's[23] initial successful transthoracic esophagectomy in 1913, the esophagus, hitherto considered operatively inaccessible, has attained prominent status in the surgical domain. A total of several hundred esophageal operations have been reported to date in the literature from a number of clinics.[25, 55] It is well established that the viability of enteric segments involved in various surgical technical procedures is primarily dependent on maintenance of an adequate circulation.[11, 15-18, 26, 27] Consequently, accurate knowledge of the origin and distribution of the vasa propria of the foregut may prove an invaluable asset in the advancing field of esophageal surgery. This survey is, in the main, concerned with the surgically relevant and practical details of the arterial blood supply of the gullet.

HISTORICAL

The arteries of the esophagus are much less well described in the literature than are the esophageal veins. No pertinent specific arterial studies in the English language appear to have been published during the past century, although Kegaries[28] a decade and a half ago investigated the esophageal venous plexuses. A few random and incidental notes on the esophageal circulation, however, appear in scattered fashion in several monographs on thoracic surgery and anatomy.

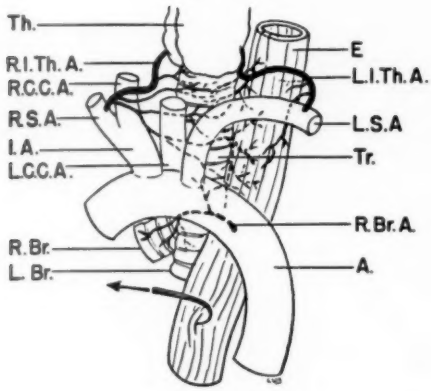
* Presented in part as a Scientific Exhibit at the May, 1948, Annual Meeting of the New York State Medical Society. Submitted for publication June, 1949.

Gossart[29] and Demel[30] provide the only fairly comprehensive references during the past 50 years. Both authors, however, conducted their studies about a quarter of a century ago, long before modern resective approaches to the esophagus had become relatively popularized. Before this, Luschka,[31] Cruveilhier,[32] Sappey,[33] and Henle[2] among the older anatomists reported the first important findings concerning the esophageal branches of the aorta; subsequently Testut,[13] Poirer and Jonnesco,[4] and Rouviere[74] concerned themselves to a limited extent with this subject, adding several facts apparently from original sources. More recently, Leriche,[34] Hovelacque,[35] Gregoire,[36, 37] Vasconcelas,[38] and Sauerbruch,[39] individually contributed several notations concerning the surgical anatomical significance of these arteries. The exhaustive treatises of Adachi[10] and Do Rio Branco,[41] although primarily concerned with other vascular structures, yield brief original data. Lately, Horine,[42] Berry,[43] Hudson,[44] Cauldwell[45] and their co-workers, studying variously the pulmonary, coronary, and bronchial circulations have included several details concerning the esophagus. Parker and Brockington,[80] and others, utilizing experimental surgical procedures in animals, particularly dogs, have incorporated several conclusions concerning the esophageal circulation in their papers. However, Noer[81] has warned that comparisons between animals and human beings require close scrutiny as to their validity because of markedly varying arterial patterns in the alimentary systems of differing species.

METHODS

The following survey of the arteriae gulae is drawn almost entirely from our own dissection material. In a number of instances our accord or disagreement with previous authors in respect to specific details is cited. Fifty bodies were dissected, but some of our percentages are from a somewhat smaller number since, in certain instances, only one region under investigation was thoroughly worked out. The anatomic studies were performed during the course of complete necropsies on the refrigerated bodies of persons who had been dead less than two days. No bodies were included in which pathologic changes or extreme obesity existed of such a nature as to grossly obscure the cervical, thoracic, or upper abdominal structures. Arterial color mass was as a rule not utilized in following the course of proximal larger vessels. The detailed distribution of small branches of the arteriae propriae of the esophagus, trachea, bronchi, thyroid, and upper stomach, not easily and obviously identifiable by gross dissection, was generally determined by means of cannulation with blunted hypodermic needles and injection of India ink from a 5 cc. syringe. In several cases, for purposes of radiographic or three dimensional visualization, the larger arteries were injected with a thin barium sulfate suspension or a red vinylacetate plastic color mass. Almost all specimens were sketched and tabulated during dissection and discarded within one or two days, since facilities for preservation were seldom available.

FIG. 1



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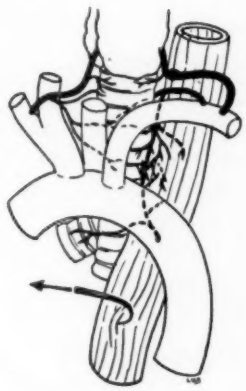

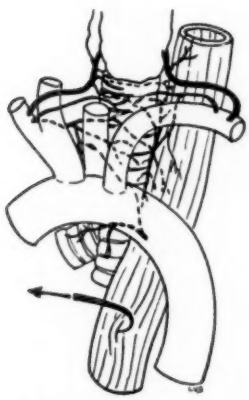

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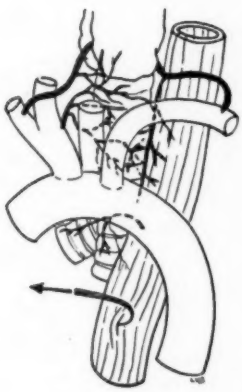


FIG. 4

FIG. 1.—Pars cervicalis, typical pattern: The right inferior thyroid supplies a greater number of branches than the left. Posterior esophageal twigs are relatively few and small. Many tracheal and esophageal twigs arise as bifurcations from the common tracheo-esophageal artery lying in the groove. Anastomosis with ascending branch of the right brachial artery is usual.

FIG. 2.—Pars cervicalis, common variant: The left esophageal arteries stem in the main directly from the left subclavian and are somewhat increased in number. Anastomosis between tracheo-esophageal arteries and right bronchial is present.

FIG. 3.—Pars cervicalis, common variant: The majority of esophageal branches to the pars cervicalis come from direct right and left branches of subclavian artery. A few upper twigs are contributed by the inferior thyroids.

FIG. 4.—Pars cervicalis, uncommon variant: The thyroid ima artery providing the majority of the right esophageal branches to the pars cervicalis. In this instance no gross anastomoses with bronchial arteries were observed.

Keys: Th. (thyroid), E. (esophagus), Tr. (trachea), L. Br. (left bronchus), R. Br. (right bronchus), A. (aorta), I. A. (innominate artery), R. CC. A. (right common carotid artery), L. CC. A. (left common carotid artery), R. S. A. (right subclavian artery), L. S. A. (left subclavian artery), L. I. Th. (left inferior thyroid artery), R. I. Th. A. (right inferior thyroid artery), R. Br. A. (right bronchial artery). (Note: Broken lines indicate course behind structures shown.)

FIG. 5

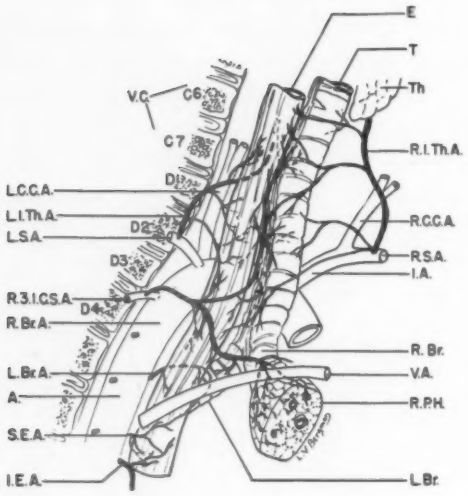
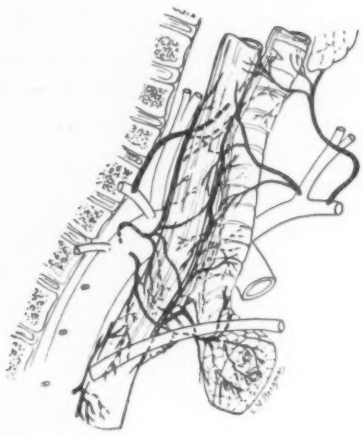


FIG. 6



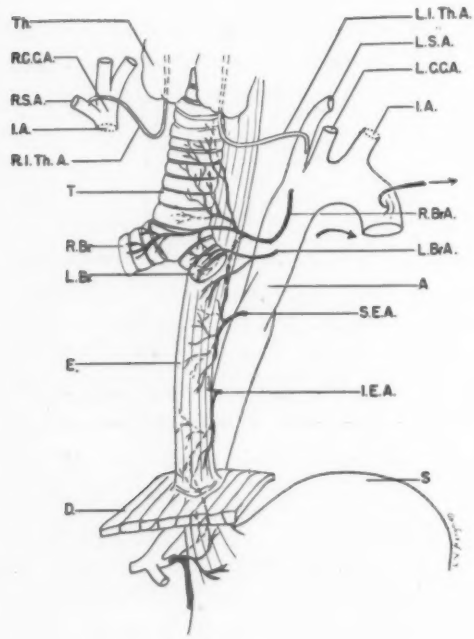


FIG. 8

FIG. 7

FIG. 5.—Pars bifurcalis, usual pattern: The right bronchial artery, originating as it frequently does, from the right third intercostal artery, passes behind the esophagus. A vertical tracheo-esophageal artery in the tracheo-esophageal groove is formed by anastomosis between the descending branches of the right inferior thyroid artery and the ascending branches of the right bronchial. The right bronchial also anastomoses, in this specimen, with the superior esophageal artery.

(*Legend continued on opposite page*)

GENERAL CONSIDERATIONS

The esophagus in this study is described as divided from above downward into the following four segments, the names of which are essentially self defining: 1. Pars cervicalis; 2. Pars bifurcalis (that portion adjacent to the aortic arch and tracheal bifurcation); 3. Pars thoracalis; 4. Pars abdominalis.

The gullet differs from most other parts of the gastro-intestinal tract in that it is primarily a tubular musculo-membranous conduit, rather than a secretory, digestive, and absorptive organ.[20-22] As might therefore be expected, it is less liberally supplied with arteries of gross caliber and its intramural vascular plexuses are relatively sparse. Arteriae esophageae propriae, although essential for the viability of this structure, seldom exceed 3 mm. in diameter.

The circulation of these parts in the adult can be better understood after consideration of their development in the fetus. Embryologically the trachea, bronchi, and lungs, as well as the thyroid, are derived from the foregut, and as a consequence, an ultimate intimate relationship between their blood vessels and that of the esophagus ensues. Similarly, the dorsomedian part of the diaphragm originates from the cephalad segment of primitive dorsal mesentery, thus accounting for the intermingling of the esophageal and phrenic circulation.[46, 47]

The esophageal arteries proper are derivatives of the paired vitelline branches of the fusing embryonic dorsal aortae and, with the bronchial arteries, may be considered as in serial sequence with the ultimately unpaired fused coeliac, superior mesenteric, and inferior mesenteric trunks. Unlike the predominant pattern in the large and small intestines, in the absence of an adult mesentery, these arteries, as a rule, course longitudinally rather than radially, forming, to some degree, vertical anastomotic chains. The primary unbranched trunks are obscured in the connective tissue of the mediastinum and stand out clearly only when the aorta and esophagus are separated by dissection.

From a surgical point of view the esophagus is probably quite properly considered as analogous to gut elsewhere, in that the viability of segments

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FIG. 6.—Pars bifurcalis, uncommon variant: In a typical case the right bronchial artery provided only a few small twigs. Unlike the usual distribution, the larger and greater number of branches were left-sided in this instance, stemming in the main from a left-sided ascending tracheo-esophageal artery from the arch, and a left bronchial, from which an unusually small right bronchial artery springs. Several small twigs arose from the right common carotid near its origin.
Keys: V. A. (vena azygos), V. C. (vertical column), R. P. H. (right pulmonary hilum), R. 3 1. A. (right third intercostal artery).

FIG. 7.—Pars bifurcalis and pars thoracalis, typical pattern: The right bronchial artery contributes more to esophageal circulation than the left, via an ascending tracheo-esophageal artery and direct branches. The thoracic esophagus is supplied by two unpaired direct esophageal arteries, the uppermost anastomosing with the bronchials. As is characteristic, the inferior artery is larger in size.

FIG. 8.—Pars bifurcalis and pars thoracalis, common variant: A single direct thoracic esophageal artery of appreciable size is found, bifurcating into fairly large ascending and descending branches, the former rejoining the superior esophageal artery. A grossly discernible thoraco-abdominal anastomosis, found in over half the cases, exists.

involved in various surgical technical procedures must largely depend on maintenance of an adequate circulation. The numerous gossamer-thin twigs to the esophagus often encountered are, in all likelihood, of little value as collateral circulation after disruption of the sturdier esophageal arteriae propriae, although they may play an important part in the spread of infection and in metastases of malignant tissue. For this reason many fine arteriolar anastomoses that have been shown to exist between the esophageal vessels and the pericardium, heart, pulmonary veins, internal mammary arteries, and thymic vestiges are omitted from further detailed consideration in this study.

ANATOMIC FINDINGS

For the sake of brevity our observations, when possible, have been presented in statistical summary, or arranged in tabular form. Much of the descriptive material is given in association with the appropriate illustrations. The latter are semi-diagrammatic, drawn without reference to possible variations in the topographic visceral anatomy, which is schematized, since we are here concerned primarily with the regional vasculature.

I. *Pars Cervicalis:*

A. Primary supply-inferior thyroid artery (from the thyro-cervical trunk of the subclavian artery).

B. Origin of major arteries to pars cervicalis.

From inferior thyroid	34 cases
From subclavian	12 cases
From thyroid ima	3 cases
From common carotid	1 case

Almost invariably the anterior arteries are functional tracheo-esophageal vessels, coursing and bifurcating in the groove and giving branches to both structures. In about two-thirds they are more voluminous on the right. Posterior vessels are generally smaller and few in number, and are more apt to run transversely.

C. Anastomoses or collaterals (grossly traceable and presumably surgically significant).

	Left	Right
With sup. thyr. A. A.	1 case	.....
With bronchial A. A.	8 cases	2 cases
With aortic twigs	5 cases	33 cases
With each other	 5	.....

D. Accessory arteries.

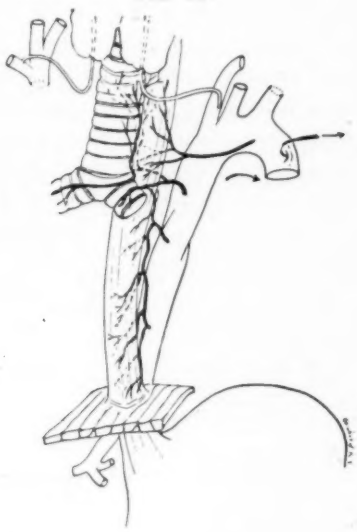
From subclavian	9 cases
From aorta	4 cases
From carotid	2 cases
From vertebral	1 case

II. *Pars Bifurcalis:*

A. Primary supply-bronchial arteries (from aorta or the right third or fourth intercostal artery).

FIG. 9

FIG. 10



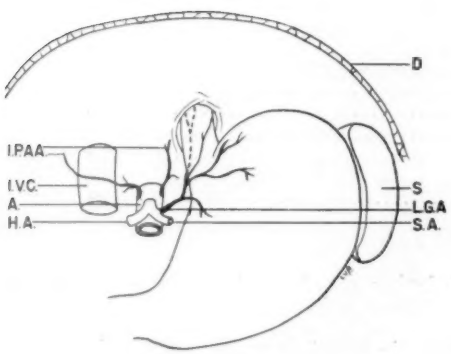


FIG. 11

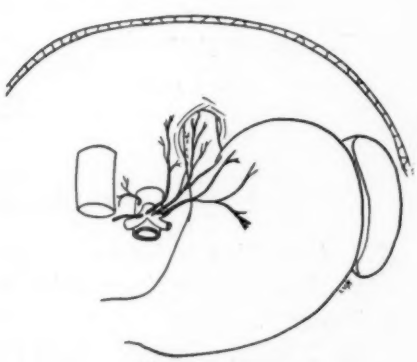


FIG. 12

FIG. 9.—Pars bifurcalis and pars thoracalis, infrequent variant: A third primary esophageal artery of appreciable size stems directly from the thoracic aorta. In this instance the left superior bronchial artery has a common origin with the right, and a left inferior bronchial artery, supplying several fair-sized esophageal branches, is seen. This is a fairly common pattern for the bronchial arteries.

FIG. 10.—Pars bifurcalis and pars thoracalis, uncommon variant: A fairly large direct esophageal artery arises from the concavity of the aortic arch. The superior and inferior esophageal arteries proper are joined in an anastomotic arc lying alongside the aorta. From this, in an unusual radial pattern replacing the customary longitudinal anastomotic chain, numerous vasa propria branch to esophagus.

Key: C. A. (coeliac axis), S. (stomach), D. (diaphragm), R. and L. Br. A. (right and left bronchial arteries), S. and I. E. A. (superior and inferior esophageal arteries).

FIG. 11.—Pars abdominalis, typical pattern: A cardio-tuberous branch of the left gastric artery provides several branches to the infradiaphragmatic segment of the esophagus. A posterior ascending twig is seen, entering into an anastomosis with the inferior thoracic esophageal artery.

FIG. 12.—Pars abdominalis, common variant: The esophageal branches arise directly from the coeliac axis, adjacent in this instance to the origin of an accessory hepatic artery. The left inferior phrenic artery arising from the coeliac axis supplies a few twigs to the posterior wall of esophagus. No thoraco-abdominal anastomosis is seen.

B. Origin of major arteries to pars bifurcalis

From bronchial arteries	47 cases
From aorta and arch	3 cases

In over two-thirds of the cases, a greater number of arterial branches are directed along the left side of the esophagus in this region, those from the right bronchial most frequently passing behind the esophagus. Twigs are found, however, at both right and left esophageal borders, where they branch into ascending and descending limbs supplying both the intrathoracic trachea and bifurcation and the esophagus to as far as 5 to 8 cm. below the aortic arch. The importance of the bronchial contribution at this level is generally overlooked.[1-14, 58-79]

C. Anastomoses or collaterals: (Grossly traceable and presumably surgically significant).

	Left	Right
With inferior thyroid A	6 cases	29 cases
With subclavian A	2 cases	4 cases
With carotid A	3 cases	1 case
With intercostal, third	2 cases	.. cases
With aortic twigs	 12	.. cases
With thoracic esophageal A. A	6 cases	17 cases

D. Accessory arteries.

From aorta and arch	23 cases
From innominate artery	4 cases
From subclavian	5 cases
From carotid A. A	2 cases
From upper intercostal A. A	6 cases
From internal mammary A. A	7 cases

III. *Pars Thoracalis:*

A. Primary supply-superior and inferior esophageal arteries (from thoracic aorta).

B. Number of major arteries to thoracic esophagus.

		1 present	2 present
Superior	Found in 46 cases	in 43 cases	in 3 cases
Inferior	Found in 48 cases	46 cases	2 cases
Accessory (lowermost)	Found in 5 cases	3 cases	2 cases

The primary aortic branches to the thoracic esophagus *below the arch are generally described as from three to seven in number.*[1-14, 58-79] *In 90 per cent of these cases, only two were found,* in most instances as a smaller upper or lesser superior and a greater or inferior esophageal artery. These vessels are almost always unpaired and arise from the anterior aspect of the aorta slightly to the right of the midline. In a few instances only one somewhat enlarged aortic esophageal artery was found.

The superior artery generally arises at the level of the T6–7 intervertebral disc and seldom exceeds 3 to 4 cm. in length. The inferior comes off some 3 to 5 cm. lower at about the T7–8 disc level and is both thicker and longer, attaining possibly 6 to 7 cm. in length. Both course to the posterior surface

of the esophagus, dividing into right and left trunks, each giving ascending and larger descending branches. Terminal branches enter the pulmonary ligaments and pericardium. A variable number of additional delicate vascular strands, so fine as to appear inconsequential from a surgical standpoint, are always encountered. In about 7 per cent a radial pattern of vasa propria from an anastomotic arch between the superior and inferior arteries obtains.

C. Anastomoses (grossly traceable and presumably surgically significant).

	Superior		Inferior
With left bronchial A. A.	5 cases		1 case
With right bronchial A. A.	16 cases		3 cases
With inferior phrenic	.....		6 cases
With left gastric	1 case		28 cases
With each other	.....	19	.....

D. Accessory arteries.

From lower intercostal A. A.	3 cases
From coeliac axis	2 cases
From aorta	5 cases

IV. *Pars Abdominalis:*

A. Primary supply-left gastric artery (from coeliac trunk).

B. Origin of major arteries to pars abdominalis.

From left gastric	43 cases
From inferior phrenic	9 cases
From aorta	3 cases
From gastrohepatic (accessory hepatic)	9 cases
From splenic	1 case
From coeliac axis	8 cases

The left gastric artery, or its cardiotuberous branch, fairly constantly supplies a number of twigs, usually from two to four, to the infradiaphragmatic segment. The thoraco-abdominal anastomosis, present in grossly appreciable caliber in about two-thirds of cases, is generally between a posterior abdominal esophageal branch and the inferior thoracic esophageal artery. The central branches of the inferior phrenic arteries often form a circle about the hiatus, but these arteries appear to communicate directly with the esophageal vasculature in no more than 20 per cent of cases. A true infra-hiatal peri-esophageal arterial circle is seldom observed.

C. Anastomoses (grossly traceable and presumably surgically significant).

1. Left gastric, coeliac axis, or gastro-hepatic.

With superior esophageal	1 case
With inferior esophageal	28 cases
With gastric arteries	24 cases
With splenic	5 cases
With hepatic	8 cases
With renal, suprarenal	1 case
With each other	7 cases

2. Inferior phrenic.

With inferior esophageal	6 cases
With gastric arteries	4 cases
With splenic	2 cases
With hepatic	2 cases
With renal, suprarenal	5 cases

D. Accessory arteries.

From coeliac axis	11 cases
From hepatic, accessory hepatic A.	7 cases
From splenic	2 cases
From aorta	6 cases

CLINICAL AND SURGICAL IMPLICATIONS

The surgical applications of the foregoing observations may now be commented on briefly and several guarded conclusions drawn. The indications for esophageal surgery in accordance with current trends are primarily the several conditions here listed. Esophagectomy and esophagogastrostomy are carried out for carcinoma of the gullet and gastric cardia,[25, 55] benign tumors, extensive strictures,[52, 53] and, relatively recently, lower esophageal varices.[55] Esophagogastrostomy and esophagoplasty are performed, in the main, for congenital atresia and tracheofistula,[50, 51] diverticuli,[57] the narrower strictures, and in some instances of achalasia or cardiospasm.[54]

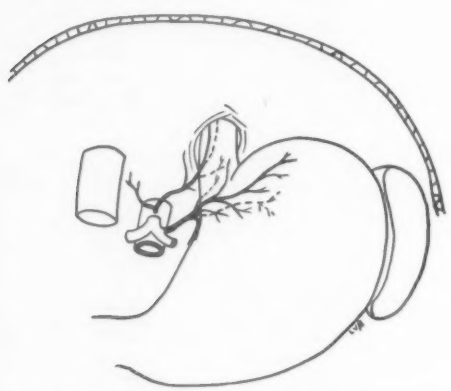


FIG. 13.—Pars abdominalis, infrequent variant: The left inferior phrenic artery, arising in a common stem with the right, largely replaces the left gastric in supplying the abdominal esophagus and enters into the thoraco-abdominal anastomosis.

The somewhat high operative mortality expected in this type of surgery may be partly attributed to impaired healing of suture lines; just as inadvertent devascularization of small intestinal or colonic segments may result in grave consequences in abdominal entero-anastomosis. The major direct complications secondary to surgically produced ischemia are diastasis and leakage leading to mediastinitis. Closely paralleling an occasional late complication in biliary and intestinal surgery, ischemic necrosis may also eventuate in delayed stricture formation rather than early perforation. This unsatisfactory outcome, now probably seen more often than early sloughing and anastomotic leakage, results in the late progressive obstruction frequently observed in patients surviving operation for several months in whom the recurrence of neoplasm is not found at necropsy.[84]

In the pars cervicalis the major blood supply is derived from below as bifurcating twigs from common tracheo-esophageal arteries in the tracheo-esophageal groove. Extensive separation of the upper esophagus from the

trachea results in the laceration of a large number of these. The collateral supply, via the superior thyroid, *etc.*, is meager. The frequent sloughing of the exteriorized cervical esophagus reported[25, 55] in the classical Torek esophagectomy and the notable failure of many attempted anastomoses with skin tubes may in large part be due to ischemic necrosis of this nature. In operating upon the higher diverticuli it is suggested that the esophagus be displaced from its bed as little as possible to preserve the circulation intact.

At the pars bifurcalis, extensive mobilization may lacerate both bronchial arteries, and, in a number of cases, the tracheo-esophageal anastomotic arc between the bronchial and inferior thyroid arteries. In about half the cases no appreciable compensatory collateral circulation appeared demonstrable. Consequently in operating for cancer in the mid-thoracic esophagus, mobilizing the

Esophageal Arterial Patterns in Relation to Surgical Procedures

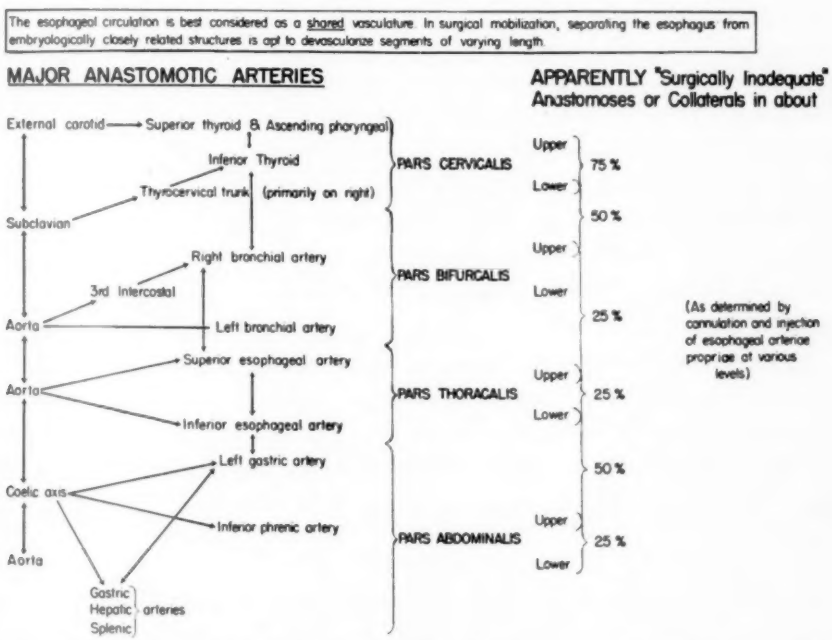


FIG. 14.—Key: S. (spleen), H. A. (hepatic artery), S. A. (splenic artery), L. G. A. (left gastric artery), I. V. C. (inferior vena cava), I. P. A. (inferior phrenic arteries).

esophagus and bringing it anterior to the arch strips it of its blood supply in a large number of cases, probably contributing to the high mortality (probably about 50 per cent) of this procedure. Later stricture formation and recurrent obstruction, an all too frequent, albeit delayed, complication, is probably attributable to partial devascularization and gradual necrosis with the familiar end result of obliterative fibrosis. An approach in which a high gastro-esophageal extra-thoracic or cervical anastomosis may be performed without greatly displacing the esophagus from the trachea may be preferable, and has recently been described by both Garlock[82] and Sweet.[83]

At the pars thoracalis, the aorta and esophagus may be gently separated for several centimeters, as a rule without marked devascularization. However, we believe that especial care should be taken to avoid tearing the two esophageal arteriae propriae coming off in the upper third, unless resection is intended. Simple dislocation of the lower thoracic esophagus from its bed, if these arteries are not avulsed, need not interfere greatly with the blood supply. Collateral circulation from above is fairly adequate for short segments left for anastomosis. In operating for stricture or infantile atresia, if an end-to-end anastomosis of esophagus is contemplated, minimal separation from the aorta is advisable. If this is not feasible without extensive mobilization, resection of the involved area and trans-thoracic esophagastrostomy would appear indicated.

At the pars abdominalis, if the left gastric artery is severed to facilitate gastric mobilization, and the complete length of the thoracic esophagus is extensively freed, the lower esophagus may be seriously devascularized. In the writers' judgment the inferior phrenic artery may not always be relied upon, since it contributes relatively little to the blood supply here and anastomoses between the bronchial and left gastric arteries are rare. For these reasons, in low esophagogastrostomy for cardiospasm or stricture, ligation of the left gastric artery would seem inadvisable if it can be avoided. In total gastrectomy via the abdominal approach, the esophageal branches arising from the coeliac plexus should be preserved, if possible. Many of the failures in attempted total gastrectomies of a decade or more ago, when adequate viable esophagus was not brought down, were quite possibly due to ischemic diastasis of the anastomotic suture lines. If the hiatus is opened widely and the esophagus dissected free without regard for the regional supplying arterial twigs, the lowermost segment of esophagus will have an impaired blood supply and should, we believe, often be resected rather than utilized for anastomosis.

SUMMARY

The arterial blood supply of the esophagus found in dissecting 50 bodies has been described. The anatomic configurations and variations are detailed with particular reference to their surgical significance. The premise is offered that the esophageal circulation is best considered as a *shared* vasculature, and that due care must be taken during surgical mobilizations in separating the esophagus from such embryologically related structures as the trachea, bronchi, and diaphragm, lest the freed segments be devascularized to a degree incompatible with reparative processes. The possible etiologic role of ischemic necrosis in early diastasis and leakage, or in delayed obliterative fibrosis and stricture, of reconstructive esophageal anastomotic suture-lines at various levels is considered. Methods of minimizing injury to the blood supply and thereby preventing devascularization during esophageal surgery are suggested.

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SIMULTANEOUS CERVICAL AND THORACIC APPROACH FOR RESECTION OF CARCINOMA IN THE UPPER FOURTH OF THE ESOPHAGUS*

REPORT OF A CASE WITH CERVICAL ESOPHAGOGASTRIC ANASTOMOSIS

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Removal of tumors in the upper fourth of the esophagus with primary re-establishment of esophagogastric continuity has been described recently,[1, 2] but the rarity of such reports prompts our description of a new technic which we have used successfully in one instance. The method involves simultaneous exposure of the esophageal lesion by a cervical and a thoracic approach. After completion of the resection the mobilized stomach is carried upward through the thorax posterior to the left subclavian and carotid arteries into the neck for anastomosis to the esophagus through the cervical incision.

TECHNIC OF OPERATION

The patient is placed on his right side, and the left hemithorax and left side of the neck are prepared and draped to allow simultaneous access to either area (Fig. 1). The left upper extremity is completely enclosed in sterile drapes to include the axilla and point of the shoulder, permitting the extremity to be moved freely to various positions as demanded by the stages of the dissection. During the intrathoracic maneuvers the upper extremity is allowed to lie forward, during the cervical dissection it lies at the patient's side, and in combined maneuvers it is supported midway between these positions. By suitable placement of drapes the patient may be rotated to facilitate the cervical or intrathoracic dissection without destroying the sterility of the field.

Either cervical or thoracic exploration may initiate the procedure. The cervical incision lies along the anterior border of the left sternomastoid muscle above the suprasternal notch, and the dissection is carried between trachea and carotid sheath to expose the esophagus. The middle thyroid vein is divided, and the sternomastoid muscle is retracted laterally without resection of the clavicle or the first rib. By this approach the cervical esophagus and the tumor may be partly mobilized.

If the tumor appears to be removable, the thoracic approach may be employed, leaving the cervical wound open. The patient's left side and left arm are rotated anteriorly to allow placement of a long posterolateral incision over the left sixth, seventh, or eighth rib. Almost the entire length of the under-

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lying rib is resected, and the thorax is entered through the rib bed. The lung is retracted anteriorly, and an incision is made through the mediastinal pleura lateral to the left subclavian artery from the aortic arch to the apex of the chest. The subclavian artery is retracted anteriorly, and the esophagus is exposed. The tumor is identified and is mobilized by dissection from below and by working through the cervical wound (Fig. 2). After the upper esophagus and the tumor are completely freed, the remainder of the esophagus is mobilized down to the diaphragm. The phrenic nerve is crushed just above the diaphragm to facilitate the transdiaphragmatic exposure and delivery of the stomach. The diaphragm is incised anterolateral to the esophageal hiatus, and the abdomen is inspected for metastases. An extensive mobilization of the stomach is then performed which preserves only the right gastric and right gastro-epiploic vessels and the vascular arches along the curvatures. After ligation at the cardia the esophagus is divided and the proximal end covered by a rubber finger cot. The distal end is inverted into the stomach with two rows of silk sutures. The esophagus and the tumor are drawn up out of the mediastinum into the cervical wound (Fig. 3). The fundus of the stomach is then brought up to the apex of the chest behind the hilum of the lung and is passed dorsal to the left subclavian and left carotid arteries. By means of an Allis clamp passed downward from the cervical incision between the trachea and the carotid sheath the apex of the gastric fundus is drawn upward through the thoracic isthmus and forward into the cervical wound. Manipulation of the stomach from above and below permits an adequate portion of the fundus to lie without tension in the cervical wound. This allows satisfactory anastomosis of the stomach to the esophagus at the level of the isthmus of the thyroid.

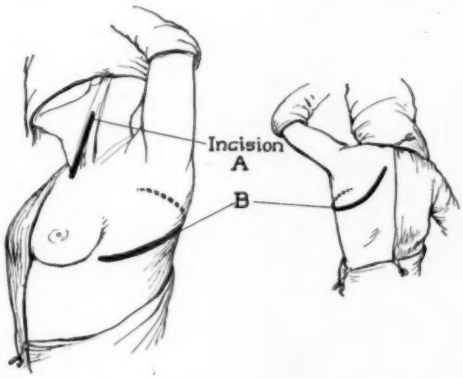

FIG. 1.—Lateral and dorsal views to show incision and method of draping.

The esophagogastric anastomosis is carried out through the cervical wound. The placement of the posterior row, consisting of interrupted fine silk sutures, is facilitated by using the distal esophagus as a handle to expose the posterior esophageal wall above the tumor. After these sutures are tied an incision is made through the posterior esophageal wall and through the wall of the adjacent stomach. The posterior row of the internal layer of the anastomosis is then placed, which approximates the full thickness of the esophageal wall to that of the stomach by interrupted inverting sutures of fine silk with the knots tied inside the lumen. The incision is carried through the esophageal wall which permits the tumor and the entire length of the infracervical esophagus to be removed. The internal and external layers of the anastomosis are completed anteriorly (Fig. 4).

A small nasal catheter is passed through the anastomosis into the intrathoracic portion of the stomach for maintenance of gastric decompression during the immediate postoperative period. A Penrose drain is placed in the lower angle of the cervival wound, and this incision is closed in layers with fine silk.

While the cervical wound is being closed the stomach is anchored to the mediastinum and posterior parietal pleura of the left hemithorax by multiple interrupted silk sutures. The apical pleura is tacked securely to the fundus so as to seal off the pleural cavity. The defect in the diaphragm is closed snugly around the gastric antrum, and the chest is thoroughly irrigated with saline solution. A Foley catheter is led out posteriorly through a stab wound in the

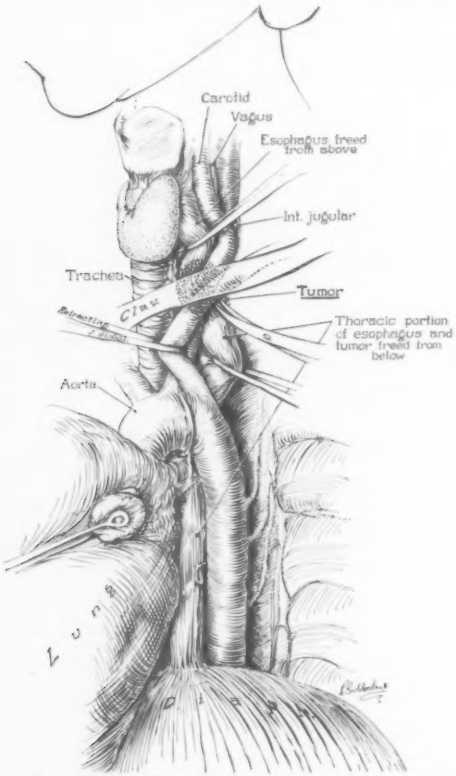

FIG. 2.—Simultaneous cervical and thoracic approach for carcinoma of upper esophagus. The esophagus and tumor have been freed from above and below.

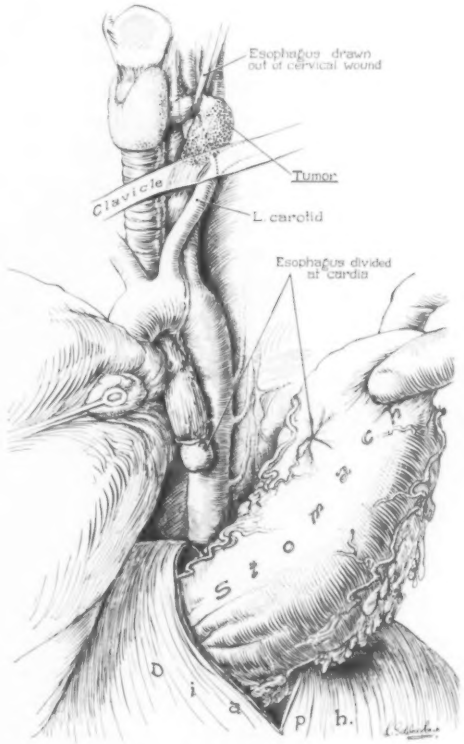

FIG. 3.—Simultaneous cervical and thoracic approach for carcinoma of upper esophagus. The esophagus has been divided and the stomach has been brought into the thorax.

ninth or tenth intercostal space for water-seal drainage. The lung is expanded by the anesthetist, and closure of the chest wall is carried out in layers with interrupted silk sutures.

CASE REPORT

S. R., a 69-year-old white woman, was admitted to the Johns Hopkins Hospital on January 17, 1949, with the complaint of difficulty in swallowing of 8 months' duration.

Family history and past history were noncontributory. About 8 months before admission she had noticed that food seemed to "stick in her throat" and that there was a "lump in her throat" at all times. These symptoms gradually progressed in severity. Three months before entry she became unable to swallow solid food and subsequently subsisted on liquids. She had lost 14 pounds in 3 months.

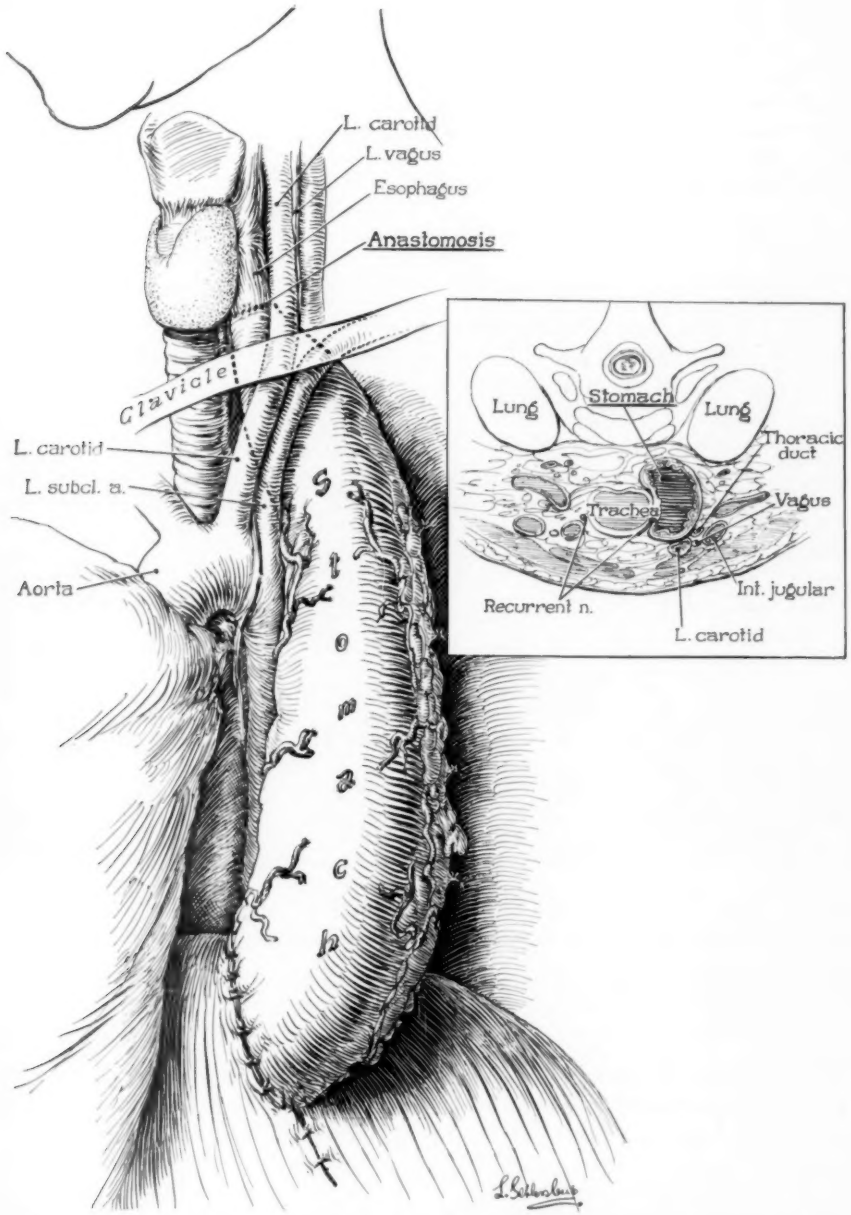

FIG. 4.—Simultaneous cervical and thoracic approach for carcinoma of upper esophagus. Completed anastomosis. Insert shows relations just below the clavicle.

Physical examination showed an emaciated little woman weighing 85 pounds. When she swallowed liquids a loud gurgling sound was audible. The heart and lungs were normal. The abdomen was scaphoid. The remainder of the examination was not remarkable.

The laboratory studies revealed a hemoglobin of 13 Gm. and normal urine. The serologic test for syphilis was negative. The serum proteins were 7.2 Gm. per 100 cc., the non-protein nitrogen was 30 mg. per 100 cc. and the chlorides were 104 milliequivalents per liter. The fasting blood sugar and serum bilirubin were within normal limits.

Fluoroscopic examination after a barium swallow showed partial obstruction of the esophagus with a sharply localized annular filling defect 2 cm. in length at the level of the clavicle (Fig. 5). Esophagoscopy showed a fungating mass obstructing the lumen of the esophagus just below the level of the inferior constrictor muscles. A biopsy of this tissue was reported as squamous carcinoma. Roentgenogram of the chest revealed no metastases. Bronchoscopic examination showed no extension of the tumor into the trachea.

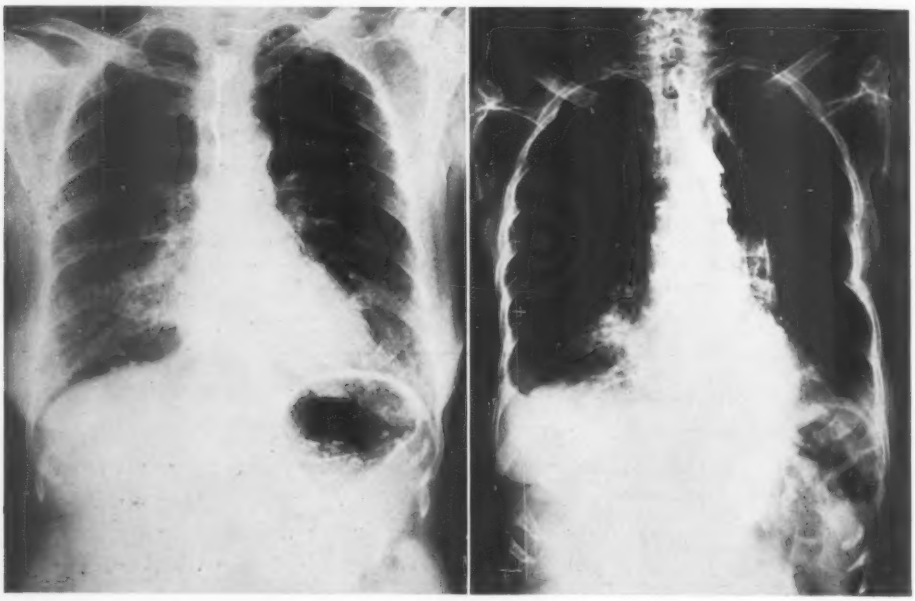

FIG. 5 FIG. 6

FIG. 5.—Reproduction of preoperative roentgenogram after barium swallow (retouched).

FIG. 6.—Reproduction of roentgenogram with barium swallow five weeks after operation. The site of anastomosis is seen above the clavicle.

The patient was placed on a high caloric liquid diet, supplemental parenteral fluids and penicillin in preparation for operation.

On January 22, 1949, operation was carried out under intratracheal nitrous oxide-oxygen and ether anesthesia; the surgical technic outlined above was used. Through a cervical incision the esophagus was exposed, and a firm tumor about 2 cm. in length was found just below the suprasternal notch. The tumor appeared to be confined to the wall of the esophagus, and a resection seemed to be feasible. Partial mobilization of the tumor was performed from above.

With the cervical wound left open, the patient's left arm and side were rotated forward, and the chest was entered through the bed of the resected left sixth rib. Working through both cervical and thoracic wounds, the operator freed the upper esophagus and tumor. The entire esophagus was then mobilized. The diaphragm was incised and the stomach mobilized and delivered into the chest. The esophagus was divided at the cardia and pulled up into the cervical wound. After the defect in the cardia was closed the fundus of the stomach was passed upward behind the hilum of the lung and dorsal to the left subclavian and left carotid arteries into the cervical wound. Esophagogastric anastomosis was carried out in the neck, and the stomach was anchored in the thorax as previously noted. There was no tension on the anastomosis, which lay at the level of the thyroid isthmus. Cervical and thoracic wounds were closed in the manner described. The patient received 1500 cc. of whole blood during an operative procedure which occupied 4½ hours.

Pathologic examination of the resected esophagus showed the tumor to be an anaplastic squamous cell carcinoma.

The patient withstood the operation very well and made a good recovery. She was maintained on parenteral fluids and constant gastric suction for 72 hours, after which time the Levine tube and the cervical drain were removed. Penicillin and streptomycin were given in full doses. The lung remained well expanded, and the catheter in the chest was removed on the fifth postoperative day. Six days after operation the patient was allowed water by mouth, and the following day she took a liquid diet. Her subsequent course was uneventful. The wounds healed per primam, and she was able to take a full soft diet by the tenth day after operation. Laryngoscopic examination showed no weakness of the vocal cords. Roentgen examination of the esophagus and stomach after barium swallow showed slight constriction at the esophagogastric anastomosis but no delay in passage of barium through the anastomosis and satisfactory emptying of the intrathoracic stomach* (Fig. 6). The patient was discharged from the hospital on February 14, 1949. Since discharge she has eaten a regular diet without restriction. There has been no subjective or objective difficulty in swallowing and no regurgitation. At times after meals she experiences a sense of fullness referred to the epigastrium and left costal margin.

COMMENT

The anatomic relations of the upper fourth of the esophagus limit the extent of radical resections of tumors in this area. Even though the likelihood of permanent cure may be slight, it appears justifiable to resect such tumors if esophagogastric continuity can be re-established, thereby enabling the patient to swallow satisfactorily for the remainder of his life.

The procedure described offers certain features which facilitate the resection of tumors of the esophagus lying above the aortic arch and expedite the cervical esophagogastric anastomosis following the resection. The draping permits simultaneous access to the upper esophagus from the neck and from the thorax. The advantages of such a joint approach have been stressed recently by Naughton Morgan[3] in discussing his simultaneous abdominal and perineal approach to carcinoma of the rectum. By using a combined cervical and thoracic approach the high-lying esophageal lesion may be mobilized carefully by sharp dissection under direct vision, thus avoiding injury to the great vessels, the trachea, the thoracic duct, the vagi, and the left recurrent laryngeal nerve. After resection of the esophagus and mobilization of the

* Addendum: Repeat examination 8 months later showed good function.

stomach the fundus of the stomach may be passed upward into the neck from below and maintained in proper position under direct vision while the esophagogastric anastomosis is performed from above. During the latter portion of the anastomosis the diaphragm may be repaired and the chest wound closed, so that completion of the esophagogastrostomy leaves only a simple closure of the cervical wound to be done. Alternately, the thorax may be left open during the anastomosis to allow final inspection of the transplanted stomach for circulatory integrity or to manipulate a Levine tube through the anastomosis into any desired position in the thoracic stomach. Such a tube may be helpful in preventing postoperative gastric dilatation.

When the fundus of the stomach is passed upward into the neck dorsal to the left subclavian and left common carotid arteries, there is no need to resect the clavicle or the first rib as recently suggested.[4] There appears to be adequate space in this dorsal compartment of the thoracic inlet to permit the passage of the elongated gastric fundus with no untoward compression. The relations of the fundus to the structures at the thoracic inlet are depicted in the accompanying diagram (Fig 4).

The level of the thoracic incision in this procedure need not be as high as when an intrathoracic esophagogastric anastmosis is contemplated for carcinoma of the second fourth of the esophagus. Since the anastomosis in the procedure described is performed through the cervical wound, thoracotomy at the level of the eighth rib would give adequate exposure for the intrathoracic dissection and would facilitate the transdiaphragmatic mobilization of the stomach.

Within the last year both Garlock[1] and Sweet[2] have suggested plans for surgical management of carcinoma of the upper fourth of the esophagus with cervical esophagogastric anastomosis. The procedure herein described may offer some technical advantages which will facilitate the operative handling of these difficult lesions. It has been suggested that radical removal of cervical lymph nodes be done as a complement to the removal of high-lying esophageal carcinomas. This suggestion was not followed in the case reported since we considered this to be a palliative resection. If subsequent experience with this procedure indicates the possibility of cure of well localized carcinomas in the superior mediastinal segment of the esophagus, then radical dissection of the cervical nodes might be advantageously added to the operative plan.

Aside from its application to carcinoma of the upper fourth of the esophagus, this technic of cervical esophagogastric anastomosis should be adaptable for patients with extensive benign structures of the esophagus and for infants with esophageal atresia who have been treated by preliminary cervical esophagostomy and gastrostomy. In such patients it offers one solution to the many unpleasant features of antethoracic esophagoplasty.

SUMMARY

A method is described for resection of carcinoma of the upper fourth of the esophagus by a simultaneous cervical and thoracic approach. Esophago-

gastric continuity is re-established by bringing the mobilized gastric fundus upward through the thorax posterior to the left subclavian and carotid arteries into the neck for anastomosis to the esophagus through the cervical incision. The clavicle and the first rib are not disturbed.

A case is reported in which the method was employed with a satisfactory result.

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CONTINUOUS LUMBAR SYMPATHETIC BLOCK FOR THE TREATMENT OF ACUTE ARTERIAL OCCLUSION AND OTHER VASCULAR DISEASES OF THE LOWER EXTREMITY*

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A variety of peripheral vascular diseases of the lower extremity have been successfully managed with a new and previously unreported technic for continuous lumbar sympathetic block. It is the purpose of this communication to describe the technic and report the results obtained with it.

The method for continuous lumbar sympathetic block which was used is an outgrowth of the work of many investigators. Hingson and Southworth[1] first described continuous caudal anesthesia. Siever and Mousel[2] substituted the indwelling catheter for the malleable needle. Touhy[3] modified this so that a smaller catheter could be used, and applied this small catheter technic to spinal anesthesia. Block and Rotstein[4] and Posner and Buch[5] reported at about the same time the idea of maintaining caudal anesthesia with a continuous drip of 1 per cent and 2 per cent procaine respectively. Benson[6] and Hingson and Southworth[7] have used continuous caudal anesthesia for relief of vasospasm in peripheral vascular disease.

Recently, Ruben and Kamsler[8] reported successful lumbar sympathetic block without sensory or motor block by the intermittent injection of dilute anesthetic solutions through an indwelling catheter in the sacral canal. This method produced good results in thrombotic occlusion of the veins, but was of no value other than pain relief in organic arterial disease. It had the further disadvantage of requiring too much professional supervision to be widely applicable. Analysis by the author[9] of more than 100 lumbar sympathetic blocks by way of the caudal canal established the idea that selective block of the sympathetics without somatic involvement could be achieved by placing dilute solutions of local anesthetic agents in the caudal canal. In this communication it is suggested that the continuous application by a drip technic of a dilute agent will produce better lumbar sympathetic block than other methods so far reported.

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TECHNIC

A spinal catheter (size 3.5F) is inserted 5 to 6 cm. into the epidural space through the sacral hiatus. This procedure has been described in detail elsewhere.[8] Ten cubic centimeters of 1 per cent procaine are injected through the catheter. The catheter is then connected to a 1000 cc. flask of 0.1 per cent procaine in physiologic saline solution by way of an ordinary intravenous drip infusion set. The bottle is hung 30 inches or more above the mattress of the bed, and the flow is regulated at 6 to 20 drops per minute, depending on the age and condition of the patient.

After the point of entrance of the catheter through the skin has been sealed with collodion, the area is isolated from the anus with adhesive tape over gauze, and the catheter is taped to the skin to prevent its being pulled out.

The patient is instructed to lie on his side with the affected leg down as much as possible, turning to his back only for occasional rest periods. The solution depends on gravity to reach the rami communicantes in the peridural space. For this reason the patient must lie with his affected leg dependant, and must not sit up, or be placed in Fowler's position. Three hundred thousand units of procaine penicillin are given daily during the treatment for prophylaxis against infection at the catheter site.

It is usually necessary to increase the strength of the procaine solution to 0.3 per cent, 0.5 per cent and even 1 per cent in cases where treatment must be prolonged. The nerves seem to become resistant to block by the weaker solution with constant exposure to it. This may be a form of physiologic adaptation.

The continuous block is maintained for as long as seems clinically necessary. There are no set times for this, but it has been found that thrombophlebitis requires a minimum of 24 hours, and one case was treated for 164 hours continuously. When the catheter is removed a sterile dressing is applied to the site of entrance. If there is any sign of inflammation, hot wet dressings are applied. There have been no infections which failed to respond at once to this simple measure. The sacral area is tender and a little sore for 24 to 48 hours after discontinuing the treatment.

RESULTS

From March, 1948, to March, 1949, 48 patients with various peripheral vascular diseases of the lower extremity were treated with this new method of continuous lumbar sympathetic block. For clarity and convenience in tabulating the results, the 48 cases have been divided into four major groups which will be described separately.

1. *Acute arterial occlusion due to an embolus or thrombus.* This most dramatic of peripheral vascular diseases may be treated in several ways. The most certain of these is embolectomy, but the patient is usually in such poor physical condition that the undertaking of this operation is unduly hazardous. Anticoagulant therapy to prevent retrograde clotting and build-up of the thrombus or embolus must be used. Physical therapy measures have been

tried. Finally, the vasoconstrictor impulses which send into spasm not only the involved vessel but perhaps many others in the involved limb as well, must be blocked. In addition to paravertebral lumbar sympathetic block, continuous caudal[7] and fractional spinal[10] anesthesia have been used.

During the period of this study, ten cases of acute arterial occlusion of the lower extremity due to embolus or thrombus were treated by continuous block. The data on these patients are presented in Table I. In two of the patients sufficient collateral circulation developed to preserve the limb. In the others,

TABLE I.—*Ten Cases of Acute Arterial Occlusion Treated with Continuous Lumbar Sympathetic Block.*

Case No.	Name	Age	Sex	Duration of Occlusion Before Block	Duration of Block in Hours*	Amputation	Time of Death after Occlusion	Remarks
1	MS	74	F	1 hour	40, 16	None	Recovered	See text
2	RB	87	M	24 hours	96, 144	None	19 days	See text
3	WL	42	M	7 hours	72	Low thigh	Recovered	See text
4	CP	74	F	36 hours	40	None	82 hours	Terminal thrombosis common iliac artery
5	JT	54	F	18 hours	28	None	72 hours	Had cerebro-vascular accident, removed catheter 24 hours before death
6	MG	74	F	36 hours	34	Bilat. Mid-thigh	12 days	Postmortem revealed arterial occlusions of the abdominal aorta and all its branches
7	SE	56	F	24 hours	40	Mid-thigh	Recovered	Block provided pain relief, Pt. diabetic
8	LJ	52	F	4 days	5	None	4 days	Postmortem showed rt. common iliac thrombosis, mural thrombi in heart, coronary occlusion
9	WA	61	M	3 days	78	Mid-thigh	8 days	Block gave pain relief. Had advanced pulmonary Tbc
10	EH	73	F	8 days	96	None	20 days	Senile psychosis

* More than one figure indicates that two separate blocks were done.

this failed to occur, either because the site of occlusion was in the common iliac artery or above, or because death from some other cause intervened before maximum improvement had been obtained. Three of these cases are described in detail since this provides the most vivid description of the changes which take place under continuous sympathetic block.

Case 1.—M. S. was a 74-year-old white woman who was admitted to the surgical ward on October 30, 1948, because of empyema of the gallbladder. This was drained under inhalation anesthesia on the following day. On the first postoperative day (November 2) she developed a left hemiplegia. Since the patient had arteriosclerotic heart disease with auricular fibrillation and mitral and tricuspid valvular insufficiency, the cerebrovascular accident was presumed to be due to an embolus. By November 8 she had almost recovered from the hemiplegia. At 9 P.M. on this day she complained of a sudden sharp pain in the right leg which was found to be cool from the mid-thigh to the knee, and cold below the knee. No pulses were palpable below the femoral, and a diagnosis of right femoral arterial embolus was made.

One hour after the embolization, a catheter was placed in the caudal canal, and 30 cc. of 1 per cent procaine were injected through it. Pain relief was almost immediate. The

catheter was then connected for continuous sympathetic block with 0.1 per cent procaine by drip. Papaverine was given intravenously, 60 mg. every 8 hours for 48 hours and heparin was given intramuscularly, 50 mg. every 6 hours for 30 hours. After 19 hours of this therapy the right leg was warm to the toes and equal in temperature to the left leg. The block solution had been strengthened to 1 per cent metycaine. The block was stopped after 40 hours, during which 750 cc. of 0.1 per cent procaine followed by 350 cc. of 1.0 per cent metycaine were run into the epidural space through the caudal catheter.

Sixty hours after discontinuance of the block (November 12) pain again appeared in the right leg, which was found to be cold, cyanotic and edematous to a point 2 inches above the knee. Continuous lumbar sympathetic block was again started. After 2 hours the pain stopped, and the leg was warm to a point 2 inches below the knee. After 16 hours of the second block, there was no discoloration, and only the foot was cool. The block was discontinued. Five hundred cc. of 1 per cent procaine had run in. On November 14, the prothrombin time was 100 per cent, so that Dicumarol was given until November 16, when the prothrombin time had dropped to 44 per cent. Although the patient subsequently suffered two episodes of severe substernal pain with apprehension, she gradually recovered, became ambulant, and was discharged to her home on December 23. She had no further trouble with her leg.

Case 2.—R. B., an 87-year-old white male, was admitted to the medical ward with a chief complaint of "pain in my back and my legs are numb." On March 11, 1948, at 8:30 P.M. he had a sudden sharp pain in the back which radiated down the midline to the sacrum. This pain was constant for several hours, and then subsided. He was admitted to the hospital at 11:45 P.M. on the night of the episode. About one hour after the onset of pain, both legs became numb, and he was unable to move the left leg. Passive movement of it was extremely painful, and his lower abdomen was tender and sore.

Examination revealed that the patient was suffering from hypertensive cardiovascular disease with auricular fibrillation, senile emphysema, and prostatic hypertrophy with distention of the urinary bladder. The left leg was mottled with a purplish discoloration from the inguinal ligament down to the ankle. The foot was blanched, and the entire leg was cold, more so from the mid-calf downward. The peripheral pulses were absent in the left leg. A diagnosis of saddle embolus of the aorta was made, and heparin and Dicumarol therapy was started. On the morning of March 12 surgical consultation was obtained. He was considered too poor a risk for amputation of the left leg. Consultation with the anesthesia department was obtained 24 hours after the embolus had occurred. At this time the left leg was cool from the mid-thigh down, and cold below the mid-calf. There was anesthesia below the knee. Continuous sympathetic block was induced, and the patient was instructed to lie on his left side. Within 12 hours the left leg was warm to the foot, and the mottling had receded to the toes. Sensation had returned to the left leg, and the calf was exquisitely tender. There was free voluntary motion of both legs, bowel function was intact, and pin-prick sensation was normal. An indwelling urethral catheter prevented observations on bladder function. After 36 hours of continuous treatment the veins of the left leg were distended, and a questionable left posterior tibial pulse was felt. On the fourth day there was no clinically detectable difference between the two legs, and the treatment was stopped. He had received 1300 cc. of 0.1 per cent procaine in the 96 hours he was under continuous block.

After 48 hours without a block the left great toe again turned blue, and treatment was restarted. Twenty hours later the toe was again pink. Continuous block was maintained for 8 more days, when it was stopped because clinically both legs were the same in temperature and color. Twenty-four hours later the left leg below the calf felt slightly cooler to the touch than did the right. There was no other difference between the two lower extremities. The legs maintained this status for the next four days, but his heart failed rapidly, and he died on March 29 in cardiac decompensation, 19 days after the embolus occurred.

Postmortem examination was performed by Dr. Dean S. Pocock who reported in part as follows: "There is slight pale reddish purple mottling of the left thigh. Otherwise there is no discoloration of either leg or foot. The left external iliac artery is occluded by a firmly adherent clot. The point of occlusion begins 5 cm. or so proximal to the inguinal ligament, and continues distally." The clot extended down to the inguinal ligament; the vessel was not explored beyond this point.

Despite statements[11] that gangrene may be expected to follow occlusion of the external iliac artery in only 13 per cent of cases, the age of this patient, and regression toward gangrene with the early stoppage of treatment gives one the impression that the block was more important than the law of averages in preserving this patient's leg.

Case 3.—W. L. was a 42-year-old Negro male on whom an end-to-end anastomosis of the ileum was done on August 3, 1948, because of traumatic perforation of the intestine. Except for several attacks of delirium tremens, recovery was uneventful until September 7 at 6 P.M. when he noted pain in the right leg. Examination revealed a cold leg with a weak pulsation over the femoral artery, and no pulsations below this level. Penicillin, intravenous papaverine, and anti-coagulant therapy were ordered, and continuous lumbar sympathetic block was begun. The Dicumarol was continued for two days, and the papaverine for five days. The continuous block was maintained for 72 hours, during which 1000 cc. of 0.1 per cent procaine followed by 4000 cc. of 0.5 per cent procaine were given through the catheter. His pain was relieved, but ischemic gangrene appeared, and a low thigh amputation was done on the sixth day after the arterial occlusion. He was discharged from the hospital on October 3, 1948. This case is included because it illustrates failure of the method.

2. *Arteriospasm.* This condition is difficult to differentiate from arterial occlusion, and the diagnosis is made on the basis of history, operative exploration with visualization of the vessels, response to sympathetic block, or any combination of these. Four patients who had this peripheral vascular disease were treated with continuous lumbar sympathetic block. It is obvious that one must consider in all of them the possibility that the spasm was coincidentally relieved. It is not possible to run as controls untreated cases in such a group as this because the condition is rare. Hence the data are presented, and the reader may judge for himself whether or not the result would have been obtained with standard measures. Perhaps repeated paravertebral lumbar sympathetic blocks would have yielded good results. Since we were studying continuous sympathetic block, the patients were treated with it to the exclusion of other procedures. Three patients are thought to be of sufficient interest to warrant individual description.

Case 1.—R. R. was a 19-year-old Cuban sailor who walked the 90 miles from New York to Philadelphia during a three-day period when the temperature ranged from 10 to 20 degrees Fahrenheit. As nearly as the language barrier allowed us to determine, he had been outside constantly during this period, and had slept outside in the bitter cold. He was admitted to the Philadelphia General Hospital on March 12, 1948, and was first seen by a member of the Anesthesia Department on March 14. A diagnosis of bilateral frostbite with cellulitis of the legs had been made. Both feet and ankles were swollen and reddened. While the ankles were tender, the feet were almost insensitive. The toes were cold and blue and covered with blebs. He was in agonizing pain. Continuous lumbar sympathetic block was started and there was dramatic relief of pain. Within 24 hours the feet were warm. After 5 days and 6 nights of continuous treatment, during

which 1500 cc. of 0.1 per cent procaine were run in, strong posterior tibial pulses were present in both ankles. On April 7, 1948, the distal one and one-half phalanges of the right great toe were amputated, and the left great toe, including the head of the left first metatarsal, was removed. A month later skin grafts were applied to the stumps and to other denuded areas. When last seen on July 10, 1948, he was healing well, and had no circulatory difficulty in his legs.

Case 2.—F. N. was a 21-year-old white boy who fell onto a stick while playing touch football on August 9, 1948, at 10 A.M. He suffered a penetrating wound of the right medial thigh. Three hours after the accident the femoral pulse was felt above the site of injury, but there were no palpable pulses below it. The leg was cold and mottled below the site of the injury. At 2 P.M. the wound was explored under continuous spinal anesthesia by the Lemmon technic using 5 per cent procaine in spinal fluid. Anesthesia extended to the umbilicus and a total 300 mg. of procaine were given during the 2½ hour procedure. Despite the spinal anesthesia, the femoral artery was found to be pulseless and contracted in extreme spasm. Perivascular stripping of the adventitia failed to relieve the spasm, as did bathing the area with 1 per cent procaine. A thrombus was removed in two pieces through an arteriotomy. The profunda femoris was discolored and pulseless, and was tied off in order to close the arteriotomy opening. There was still no pulsation of the femoral artery. The wound was closed. Since the leg remained cold and mottled continuous lumbar sympathetic block was started at 6 P.M. The block was continued for 94 hours, during which time 4300 cc. of 0.1 per cent procaine were given. Both dorsalis pedis and posterior tibial pulses returned and the treatment was stopped. When last seen on September 14, 1948, he had normal legs with no symptoms of claudication.

Case 3.—N. C. was a 29-year-old Negro male who suffered a trimalleolar fracture dislocation of his left leg and a compound fracture of the lower tibia on the right in an automobile accident on May 12, 1948. He was treated for shock and the wound was debrided. Standard prophylactic treatment against tetanus and *B. Welchii* was given, and both lower extremities were put in plaster casts from toe to groin. Nine hours later, at 11 A.M. on May 13, the right foot was cold. The skin temperature of the right great toe was 80°F, while on the left it was 95°. In order to determine whether the patient had arteriospasm secondary to the injury or compression due to swelling under the cast, a bilateral lumbar sympathetic block by way of the caudal canal was done. The temperature of the right great toe rose from 80 to 93, and the left from 95 to 100. Four hours later the right foot was cold again. Since we thought this established a diagnosis of severe vasospasm, continuous lumbar sympathetic block was started. During the 93 hours that it was continued, 1550 cc. of 0.1 per cent procaine were run in through the catheter. He was free of pain during the block, and the feet stayed warm when the block was stopped on May 17. When last seen on November 9, 1948, he had no vascular difficulty.

3. *Chronic arterial occlusion.* This classification should include the chronic degenerative arterial diseases such as obliterating arteriosclerosis, thrombo-angiitis obliterans, and arterial obliteration secondary to diabetes mellitus. Seven cases have been placed in this group, of which six were due to arteriosclerosis obliterans, and one to arterial insufficiency of unknown origin. As yet, we have not had an opportunity of treating thrombo-angiitis obliterans or diabetic gangrene with continuous lumbar sympathetic block.

Encouraging results were obtained in this group with the new method of continuous block. Since only pain relief resulted when patients with these diseases were treated by intermittent block,[8] the fact that three patients had marked improvement with continuous drip block is a hopeful sign. The data

on the seven cases treated in this series is presented in Table II. A sidelight of interest is that all five patients who suffered from rest pain were relieved of their pain while the block was working; yet none of them had sensory anesthesia. This may indicate that the painful impulses of ischemia travel through afferent sympathetic pathways, at least in some patients.

4. *Thrombophlebitis.* Every effort was made to distinguish thrombophlebitis from phlebothrombosis in selecting patients with acute venous occlusion for treatment by continuous lumbar sympathetic block. These conditions can

TABLE II.—*Seven Cases of Chronic Arterial Occlusion Treated with Continuous Lumbar Sympathetic Block.*

Case No.	Name	Age	Sex	Diagnosis	Symptom	Duration of Block in hrs.	Result	Remarks
1	JF	64	M	Arteriosclerosis obliterans and osteomyelitis	Non-healing transmetatarsal amputation stump	146	Excellent. Healed	Bleeding granulations formed over the wound during the treatment. Healed slowly.
2	SC	62	F	Arteriosclerosis obliterans	Rest pain, legs	238	Pain relief	Died of cerebro-vascular accident 2 months later
3	FK	46	M	Arterial insufficiency, cause unknown	Intermittant claudication	92	Good	Blanching on elevation and calf tenderness were much less, and venous filling was 40 sec. before and 10 sec. after block
4	BS	77	M	Arteriosclerosis obliterans	Rest pain. Early gangrene of rt. leg	60	Poor—only pain relief	Previous amputation for same disease in other leg. Mid-thigh amputation nine days after block
5	HS	63	M	Arteriosclerosis obliterans	Rest pain, severe. Gangrene left great toe	80	Excellent. Complete pain relief	Posterior tibial and dorsalid pedis pulses returned in left foot and it became pain free and warm. Toe amputates and lumbar sympathectomy done two months later
6	VP	57	M	Arteriosclerosis obliterans and acute thrombophlebitis, left	Mid-thigh amp. 6/16/48 Pain, swelling positive Homans	142	Excellent. Complete pain relief	Left lumbar sympathectomy 1 month later. Discharged without symptoms
7	HP	64	F	Arteriosclerosis obliterans	Pain. Gangrene of two toes	36	Poor—pain relief	Patient unable to cooperate and disconnected caudal tubing, got out of bed, etc. Mid-thigh amputation done

perhaps best be differentiated by the relatively less or absent subjective disturbance in the patient with phlebothrombosis compared to the constant, aching pain complained of by the patient with thrombophlebitis. However, it is difficult in patients who are not very responsive either because of age, illness or sedation to make a distinction on this basis. It is also difficult in early cases of thrombophlebitis before the pain has become severe. Both types may have slight temperature elevations, and both have positive Homans' and Moses' signs. Two of the 27 patients treated for thrombophlebitis with continuous lumbar sympathetic block probably had phlebothrombosis. They will be described in more detail later.

The classical treatment of thrombophlebitis is that of any inflammation—heat, rest, and elevation. Many add a supportive bandage to this routine, but in the acute phase this may appreciably increase the patient's discomfort. Blockage of the lumbar sympathetic outflow of vasoconstrictor impulses was first advised by Leriche[12] and achieved its present wide acceptance in this country through the work of Ochsner and Debakey.[13] While the paravertebral lumbar sympathetic block described by these writers, and the intermittent block described by others[6-8] will almost always relieve the pain, and will, in the majority of cases, give good results, continuous drip lumbar sympathetic block has seemed to give better results. The response to this treatment has been more rapid and the good results more lasting than was seen in similar patients

TABLE III.—*Showing Twelve Cases of Thrombophlebitis with Cure Following Continuous Lumbar Sympathetic Block.*

Case No.	Name	Age	Sex	Predisposing Factor	Interval Onset to Start Rx	Interval Start Rx to Pain Relief	Interval Start Rx to Disappearance of Signs	Total Time of Block in Hours
1	GW	27	M	Gastrectomy	44 hours	Immediate	48 hours	96
2	MS	47	F	Nephrectomy	7 hours	Immediate	20 hours	36
3	BG	32	F	Septic abort.	5 days	Immediate	60 hours	73
4	GF	56	M	Chr. thrombophlebitis, 12 yrs. duration, with acute exacerbation	3 days	Immediate	33 hours	84
5	JR	34	M	Exacerbation dermatophytosis	8 hours	Immediate	38 hours	40
6	JA	29	F	Delivery	7 days	Immediate	28 hours	24
7	WE	42	M	Spontaneous	2 mos.	2 hours	36 hours	44
8	WF	62	M	Prostatic resection	4 hours	Immediate	24 hours	22
9	CW	60	M	Suprapubic cystostomy	7 hours	Immediate	24 hours	36
10	JL	65	M	Pneumonia	24 hours	Immediate	102 hours	90
11	LG	42	F	Frac. patella, splinted	4 days	Immediate	16 hours	25
12	DW	34	F	Delivery	11 days	Immediate	72 hours	96

treated with the older methods. Thus far, the incidence of recurrence and chronicity has been less, but this question can only be answered by a long range follow-up study which will be the subject of a later communication.

Thrombophlebitis is seen in adults of all ages; yet the patients in this series are readily divided into two groups. The first includes 18 patients in whom the disease appeared as a complication of surgery, pregnancy, infection or trauma; the second is made up of nine patients who were in a terminal condition from some lethal illness. Because thrombophlebitis has different implications in these two groups, the results of their treatment will be discussed separately.

Of the 18 patients in whom thrombophlebitis appeared as a complication of operation, etc., 12 became clinically well during, or almost immediately after the continuous block was stopped. The details of these 12 cases are given in Table III. Case 9, "C. W." was one of those in which we may have failed to distinguish between phlebothrombosis and thrombophlebitis. When

first seen, the patient's signs and symptoms were noted as being "somewhat doubtful subjectively" by the physician. Continuous block was begun anyway and continued for 36 hours. The signs had disappeared after 24 hours. The patient became ambulant, and was doing well when seen a week later. However, he suddenly died 11 days after completion of the treatment. After postmortem examination, the pathologist stated that the primary cause of death was cardiac failure, even though a small pulmonary embolus had been found. It is probable that this patient suffered from phlebothrombosis rather than thrombophlebitis when first seen, although the phlebothrombosis may have developed after completion of the treatment.

In addition to the 12 patients who were clinically cured after treatment, there were four who were considered improved, and two in whom no help other than pain relief was achieved. Of the four who were improved, three were postoperative patients who made no mention of circulatory difficulty when seen later for surgical, but not vascular, follow-up. One may therefore presume a good end result. The fourth patient had varicosities of long standing, and chronic severe dermatophytosis. The superficial and deep thrombophlebitis for which he was treated improved, but it would be difficult to say he was cured, since he had so much other disease in that leg. Two patients were classed as failures of the method. One was a postoperative patient who pulled his catheter out after 48 hours of treatment, at which time he was not free of the signs of thrombophlebitis. When seen in surgical clinic two months later there was no mention of vascular disease. The other patient classed as a failure had phlegmasia alba dolans of one to two months' duration following pneumonia. When 48 hours of block had produced no spectacular improvement, inferior vena caval ligation was done because it was thought by all concerned that the occlusive process was advancing into the vena cava. He made an uneventful recovery from the operation, but had some bilateral edema of the legs when last seen.

There were nine patients in terminal condition to whom continuous lumbar sympathetic block was given. These patients were treated because treatment was not withheld from any patient from whom there was the slightest possibility of obtaining enough co-operation to warrant any hope of helping him—even if that help were only relieving the pain of his thrombophlebitis in his last days. While all nine of these patients died during the hospital stay in which they were treated by continuous sympathetic block, five of them improved temporarily, while four failed to do so.

The data on these nine patients who were in a terminal condition is given in detail in Table IV. Case 8, "L. H.," who died during the block, is the second in which phlebothrombosis was mistaken for thrombophlebitis. This desperately ill 28-year-old woman had a sudden massive swelling of one leg which was thought to be a thrombophlebitis of the common iliac vein because of the severe lower abdominal pain and tenderness. The block had been in progress 30 hours when she died very suddenly of massive pulmonary embolus. At postmortem examination, in addition to the pulmonary embolus, she was

found to have tuberculous peritonitis and an occlusion of the common iliac vein which extended to the vena cava.

DISCUSSION

Complete co-operation on the part of the patient is essential to this procedure. Smoking must be given up entirely, not only by patients suffering from arterial occlusion or spasm, but also by those who have thrombophlebitis. While the deleterious effects of smoking are generally appreciated when the arteries are primarily involved, many seem to forget that the basis for many symptoms[13] in thrombophlebitis is ischemia secondary to arteriolar spasm. It is foolhardy to attempt to relieve this spasm with sympathetic blockage while

TABLE IV.—*Showing Causes and Time of Death after Continuous Lumbar Sympathetic Block for Thrombophlebitis.*

Case No.	Name	Age	Sex	Duration of Block Hours	Cause of Death	Time after Block	Result of Block
1	DM	67	M	96	Heart failure	42 days	Improved
2	SC	48	F	210	Heart failure	63 days	Improved
3	FD	71	M	36	Heart failure, uremia, senility	38 days	Improved
4	DM	45	F	82	Tuberculosis	9 days	Improved
5	DS	35	M	40	Portal cirrhosis	80 days	Improved
6	AG	65	M	125	Septicemia	11 days	Failed
7	WW	35	M	36	Peritonitis	3 days	Failed
8	LH	28	F	30	Tuberculous peritonitis, pulmonary embolus	During block	Failed
9	WM	72	M	103	Carcinomatosis	15 days	Failed

the patient adds to it by smoking. He must also stay in bed, be careful not to put tension on the tubing or catheter so as to pull it out, and lie with his affected side down as much as possible. Without these aids on the part of the patient, the method will fail. Since many of the patients subject to peripheral vascular disorders are in the older age groups in which co-operation with a new routine in strange surroundings is difficult or impossible, senility must be carefully ruled out before beginning the treatment. Incontinence of feces or urine makes the procedure impracticable.

A minimum amount of professional and nursing attention is required for patients receiving continuous drip block. The 1000 cc. flask must be changed at the most every 18 hours, and aside from this, no care other than that rendered any bed patient is required. The physician may limit his visits to two in 24 hours, although three or four allow closer attention to detail, and this gives better results. Except for the catheter becoming dislodged or the flow stopping, there have been no emergency complications. In addition to these advantages, a continuous drip technic eliminates frequent injections, special apparatus, and repeated handling of the apparatus.[5]

It is necessary, particularly when the sympathetic block must be prolonged, to avoid interference by the block with bowel or bladder function. The weak

solutions which have been used in this series of cases have blocked the lumbar sympathetic outflow without paralyzing those parts of the voluntary and involuntary nervous systems involved in urination, defecation, ordinary sensation, and motion. It is probable that such a weak solution injected as a single dose would have no appreciable effect, since it is reasonable to assume that a weak solution continuously applied by a constant drip will have a much greater effect than that same solution injected as a single dose.

Vascular occlusions are seen almost exclusively in patients who are already ill with a major affliction. They occur mainly in the aged or those made prematurely old by their disease. Observation of patients dying of tuberculosis, cardiac failure, carcinomatosis or overwhelming toxemia makes one wonder whether in these cases vascular occlusion may not be a part of the terminal picture rather than an intercurrent disease. Knisely *et al.*[14] have described "sludged blood." The motion pictures which they made of red cells settling out of the blood stream and attaching themselves to the vessel wall as the animal dies are vividly recalled as increasing vascular occlusion is observed in patients who are nearing death. That these patients should develop a vascular occlusion in their terminal period is not surprising; that many of them should fail to respond to treatment for it may almost be expected.

SUMMARY

1. After a brief summary of the highlights of the history of continuous caudal anesthesia, a new and previously unreported adaptation of the drip technic for continuous lumbar sympathetic block is described.

2. Results obtained in treating 48 patients suffering from a variety of peripheral vascular diseases of the lower extremity are described under four headings: acute arterial occlusion (ten cases), arterial spasm (four cases), chronic arterial occlusion (seven cases), and thrombophlebitis (27 cases).

3. In two patients with acute arterial occlusion the continuous lumbar sympathetic block seems to have been important in preserving the limb without resort to surgery; in many of the other cases, the results have been better than have been obtained in our hospital with other methods.

4. The method is simple to set up, requires no elaborate equipment and is safe. Since it seems to give better results than those obtainable with other methods of lumbar sympathetic block, it is hoped that others will try it. It has been found in this hospital to be a method of treatment for those patients suffering from arterial embolus who for one reason or another cannot be subjected to embolectomy.

ADDENDUM

Since this paper was submitted for publication, an additional 42 patients have been treated with this method of continuous lumbar sympathetic block. A total of 90 patients have been treated between March, 1948, and December, 1949.

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SARCOMATOUS TRANSFORMATION IN MULTIPLE NEUROFIBROMATOSIS (VON RECKLINGHAUSEN'S DISEASE)*

REPORT OF FOUR CASES

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MALIGNANT TRANSFORMATION as a complication of multiple neurofibromatosis is an extremely rare condition in any physician's experience and the literature is replete with reports of single cases, most of which were recorded prior to 1910. Sarcomatous change is one of the mysteries of the disease and the transition is a very interesting problem.

MULTIPLE NEUROFIBROMATOSIS

Multiple neurofibromatosis may be defined as a systemic disease of protean manifestations and undetermined etiology which affects the nerves primarily. It was first described by von Recklinghausen in 1882.[1]

Incidence. It is estimated to occur in about one out of 2,000 persons and has been reported in the white, black and yellow races.[2, 3] A similar condition has been reported in animals.[4]

Etiology. The cause is unknown, although numerous theories have been advanced. The most popular of these have stressed endocrine disturbances or congenital embryonal disturbances of the neuroectodermal anlage or both.[3]

It is hereditary as evidenced by the studies of Prieser and Davenport on 30 families. Some evidence of the disease, such as pigmentation or multiple tumors, was present in 43.5 per cent of the offspring. This approaches the Mendelian quotient and makes the disease a dominant characteristic. The disease reappeared in several generations without a break, with little difference in sex distribution. There was also a strong familial tendency as to the type and location of the lesions. Associated congenital and developmental anomalies have been described, such as cerebral meningocele, cranial defects, spina bifida and defects of fingers and toes.[3, 5]

There is a definite endocrine factor present. Puberty, pregnancy and menopause, periods during which there is a disturbed androgen-estrogen ratio, are frequently concerned with the early manifestations of the disease or an exacerbation of previously existing disease. In the series of cases reported by Sharpe and Young,[3] an exacerbation of the cutaneous manifestations of neurofibromatosis during pregnancy occurred in approximately 72 per cent of the cases. In over one third of the children of these pregnancies the disease developed. When pregnancy was not associated with the onset or exacerbation of the disease, its development was not noted in the offspring.

* Submitted for publication May, 1949.

Symptoms and Signs. There have been various clinical types reported, but generally there are multiple nodules along the nerve trunks and pigmentation of the skin. The nodules or neurofibromata cause symptoms depending on their size and location. Superficial or deep somatic nerves as well as sympathetic and parasympathetic may be concerned. Usually the lesions are painless, but occasionally pain from pressure occurs. The skin nodules are sessile, pedunculated, soft or elastic tumors and while they may appear during infancy or early childhood, their first appearance is more frequently recognized during puberty. The pigmentation takes the form of brown patches or "cafe-au-lait" spots, which have been variously estimated to occur in 25 to 100 per cent of cases.[5] This may precede by years the appearance of the characteristic cutaneous or subcutaneous nodules. The pigmentation is not symmetrical and does not follow the distribution of nerve roots. The pigmented areas are said to increase in number and size with age.

Mental retardation, feeble mindedness and psychic aberrations have been described. Preiser and Davenport[2] found 20 times more feeblemindedness in their series than in the normal population, and Charpentier[6] found that 63 per cent of his patients showed mild psychic defects with a tendency to depression.

Endocrine disorders have been reported, and include menstrual abnormalities, incomplete sexual development, acromegaly, cretinism, myxedema, tetany and Addison's syndrome.[7] Gynecomastia and precocious puberty have also been described.

Osseous changes have been found in the majority of the cases of neurofibromatosis.[8] All osseous changes may be explained by involvement of the bone by tumor. Scoliosis is the most frequent finding and may either be primary to vertebral involvement or secondary and compensatory to shortening in the legs. Other changes include abnormality in the growth of bone, irregularity in the outline of the shafts of long bones, pseudarthrosis of the tibia, bowing of the femurs, and subperiosteal cysts. Thannhauser[9] has presented evidence to show that osteitis fibrosa cystica disseminata or localisata (Recklinghausen) and multiple neurofibromatosis are closely allied and may even be the same disease.

Pathology. Since von Recklinghausen's original description of these tumors arising from connective tissue, there has been much controversy through the years, as to whether the neurofibromata develop from mesodermal elements of the epi-, peri-, or endoneurium or from ectodermal elements. Verocay[10] in 1910 expressed the opinion that they arose from the sheath of Schwann. This idea was furthered by Masson,[11] whose extensive study in 1942 showed that neurofibromata develop from Schwann fascicles and that fibromatous growth in neurofibromatosis may occur without later evidence of the originating schwannoglial lineage. Whorls of spindle cells, if present in the fibrous tissue, are indicative of their neurofibromatous origin. Penfield[12] in 1927 suggested that neurofibromatosis was a generalized fibrous connective tissue reaction involving both nerve fibers and connective tissue. He also stated that two

types could be differentiated; (1) the neurofibromata which show the presence of nerve fibers within the tumor and (2) a perineural fibroblastoma in which the nerve fibers of the parent nerve are found about the tumor in the capsule and do not enter the tumor. The latter are more likely to be solitary tumors. Foote[13] remarks that the tumors of this group may contain nerve fibers with sheaths, nerve fibers without sheaths and sheaths containing Schwann cells without nerve fibers. Surrounding these structures are masses of fibrous tissue. We may summarize the situation by saying that the neurofibromata show considerable variation histologically with a bizarre intermixture of nerve and fibrous elements.

The pathogenesis of the pigmented cafe-au-lait spots is stated to be a localized anatomic anomaly in the cutaneous nerve itself, producing an increase of melanin in the epidermis and differs from Addison's disease where there is a hormonal imbalance of melanin production.[9]

Complications. The complications of this disease include hemorrhage into a tumor[14, 15, 5] and malignant transformation.

MALIGNANT TRANSFORMATION IN NEUROFIBROMATOSIS

This is the most serious complication of von Recklinghausen's disease. Garre[16] found it present in 12 per cent of the patients in his series. Courvoisier[17] found 53 instances of it in 800 cases of neurofibromata; 15 were classified as pure sarcoma and the rest as myxo- and fibrosarcomas. Hosoi[18] found 65 cases reported in the literature up to 1931 and by 1939 the total had reached 75 (Charache).[19] Since then about 13 additional cases have been added.

The four patients about to be reported are quite interesting. Two were brothers whose clinical courses were carefully followed from infancy. The third patient developed a sarcoma during pregnancy.

Case 1. (J. L.) This patient was born on September 7, 1928, of Italian parents. In September, 1929, he was first hospitalized, with an egg sized, hard movable nodule lateral to the right knee. This was excised and reported to be a spindle cell sarcoma. In the light of subsequent developments this diagnosis was probably an error. The patient was given roentgen ray therapy and amputation was refused.

During the patient's second hospitalization in November, 1935, a diagnosis of von Recklinghausen's disease was made. At that time the patient's right leg was shorter than the left and his skin showed discrete coffee ground pigmentation over the arm and trunk. There were numerous subcutaneous nodules present in chains over the neck, trunk and extremities. Roentgenograms revealed exostoses on the lower part of the right femur, a punched out area in the femur, and prominence of the anterior tubercle of the tibia. Laboratory work was essentially negative.

In 1941 the patient was admitted to another hospital with an orange size mass in the left side of the neck which was growing slowly. Roentgen ray examination at this time showed necrosis of the cervical vertebrae. Biopsy revealed neurofibroma.

The patient was admitted to the Buffalo General Hospital in April, 1946, with severe pain in his right leg. An exploratory laminectomy was done because of a defect noted in the spinogram, but no tumor was found. At this time there was definite evidence of mental retardation. Colloidal gold curve was found to be 4322211 00 and the spinal fluid protein was 0.4 mg. per 100.

The patient again returned to the hospital in August, 1946. At this time there was a right gynecomastia, slight kyphoscoliosis and a large, tense, indurated tumor mass in the right popliteal space. Roentgen ray examination showed anterior bowing of the right tibia and fibula. Blood chemistry studies revealed acid phosphatase of 5 King-Armstrong units; alkaline phosphatase of 7 King-Armstrong units; serum calcium of 10.2 mg. per 100 and phosphorous of 3.7 mg. per 100. A biopsy of the mass in the popliteal space revealed a medullary sarcoma and the leg was amputated above the tumor to relieve the patient of pain. Numerous neurofibromata were found in the amputated specimen and a large sarcomatous tumor was found in the sciatic nerve near the popliteal space. The proximal end of the sciatic nerve showed no evidence of tumor.

On April 4, 1947, chest films revealed evidence of multiple sarcomatous metastases and roentgen ray therapy was begun for relief of pain.

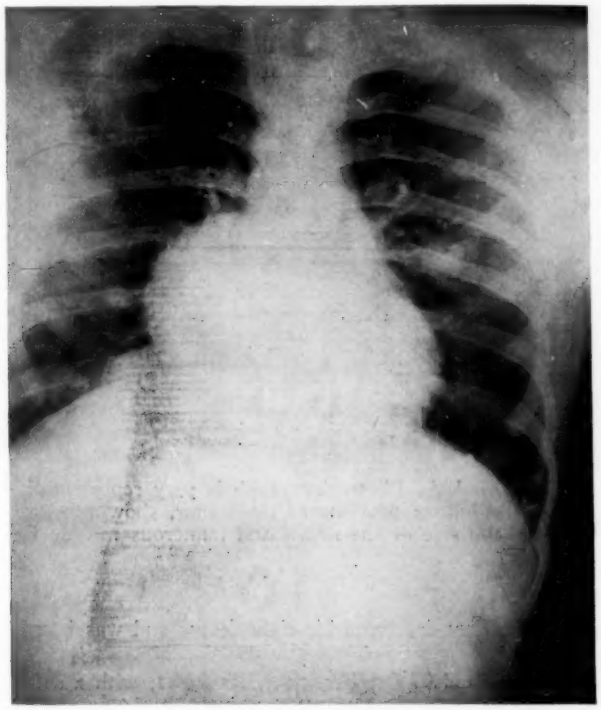

FIG. 1.—J. L. Chest film taken five months before death, showing metastases.

In July, 1947, the patient developed a walnut size right supra-clavicular tumor and within 9 weeks it was large orange size and had pushed the trachea markedly to the left. This was followed by a bloody effusion in the right pleural cavity. Dyspnea and cachexia increased in spite of repeated thoracenteses, and the patient expired on September 20, 1947. Permission for a post mortem examination was not obtained.

Case 2. (C. L.—older brother of J. L.) The patient was born on March 31, 1924. In August 1930, at the age of six, he was hospitalized for the first time because of a mass along his right tibia which was first noted 5 years previously, after a fall downstairs. It had become progressively larger and caused difficulty in walking. Physical examination revealed a marked anterior bowing of the right lower leg. In the middle third of the leg was a discrete hard area, which was freely movable and somewhat tender.

Similar areas were found above the internal malleolus. The skin revealed many scattered macules, pin head to quarter size, and brown in color. One observer likened them to Addisonian pigmentation. Laboratory determinations showed a negative Wassermann examination and a negative Bence Jones protein determination. Blood studies were as follows: serum calcium 10.4 mg. per 100; phosphorous 5.6 mg. per 100; urea nitrogen 12.6 mg. per 100; uric acid 2.7 mg. per 100; and creatinine 1.4 mg. per 100. Roentgenograms of the chest and extremities were negative except for the left humerus, which showed a 2.5 cm. diameter cystic area in the medullary portion of the middle third of the bone. Biopsy of the tumor mass in the right leg revealed a "neurogenic tumor of the type found in von Recklinghausen's disease." The patient received three treatments of roentgen ray radiation directed at the tumor and was discharged from the hospital.

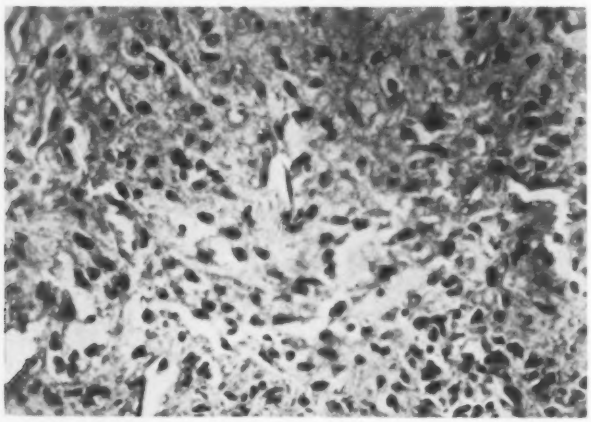

FIG. 2.—J. L. Photomicrograph is very representative of the medullary portions of the tumor, showing variations in the size of the nuclei and numerous mitotic figures. x 205.

In May, 1932, the patient fractured his right femur and was hospitalized at another hospital for several months.

He was again hospitalized in October, 1935, at age 11, with a soft, painless swelling about baseball size on the inner aspect of his right foot. The mass had increased in size during the preceding 3 years. The skin now revealed many distinct subcutaneous tumors in addition to pigmentation; they were firm, freely movable and painless. The mass on the right foot and ankle felt like a "bag of worms" and also contained several hard nodules. The right foot and leg were definitely smaller than the left. Roentgenograms revealed marked osteoporosis of both feet and hands and a cyst in the tuft of the terminal phalanx of the right big toe. Serum calcium of 8.7 mg. per 100 and blood phosphorous of 5.7 mg. per 100 were present. Biopsy of the right ankle showed a neurofibroma. He received more roentgen ray therapy to the foot with slight response in the size of the tumor and relief of pain.

An abdominal wall tumor excised in 1936 proved to be a typical neurofibroma.

He was admitted to another hospital in January, 1937, with a large tumor mass in the distal end of the right thigh posteriorly. Biopsy showed a sarcoma and the limb was amputated at the middle portion of the thigh.

In October, 1937, he was again admitted to the Buffalo General Hospital with a small grapefruit size hard mass over the left scapula. This was biopsied and reported as

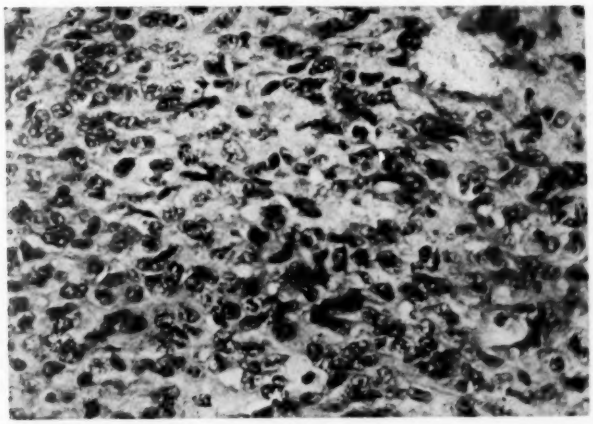

FIG. 3.—C. L. This picture depicts a rather cellular portion of the tumor, showing polygonal cells of almost endothelial appearance and in other areas a more fibroblastic pattern. x 205.

TABLE I.—*Family graph of J. L. and C. L. (Mother and Father were born in Italy)*

	Evidence of Neuro-fibro-matosis	Con-genital Defects	Endo-crine Changes	Mental Retar-dation	Osseous Changes	Malignant Change	Cause of Death
Mother—53 yrs. old. Alive and well.	Present		Acro-megalic features	Present	Negative		
Father—53 yrs. old. Alive and well.	Negative						
Children:							
1. Male—died age 9 months.	?						Pneu-monia
2. Female—died at birth	?						Pre-mature
3. Male—(C. L. in case report)—died age 13 yrs.	Present	Negative	Negative	Present	Present	1. Sarcoma rt. sciatic nerve? 2. Sarcoma over left scapula	Metas-tases
4. Female—22 yrs. old. Alive and well.	Negative						
5. Male—(J. L. in case report)—died age 18 yrs.	Present	Negative	Rt. gyne-comastia	Present	Present	1. Sarcoma rt. sciatic nerve	Metas-tases
6. Female—18 yrs. old. Alive and well.	Present						
7. Female—16 yrs. old. Alive and well.	Negative						
8. Male—14 yrs. old	Negative	Accessory left nipple					
9. Male—died age 6 months.	?	Polydacty-lism (six fingers each hand)					Pneu-monia
10. Male—12 yrs. old. Alive and well.	Present	Bilateral accessory nipples					

"a malignant tumor neurogenic in origin." Psychiatric evaluation at this time showed the patient to have an I. Q. of 76; for a calculated age of 13.6 years, the patient had a mental age of 10.1 years. A few days after admission the patient absconded from the hospital and died at home in March, 1938 (Fig. 3).

Case 3. (J. K.) This patient was a 32-year-old white female of Polish descent who was admitted to the Buffalo General Hospital on December 6, 1947. She stated

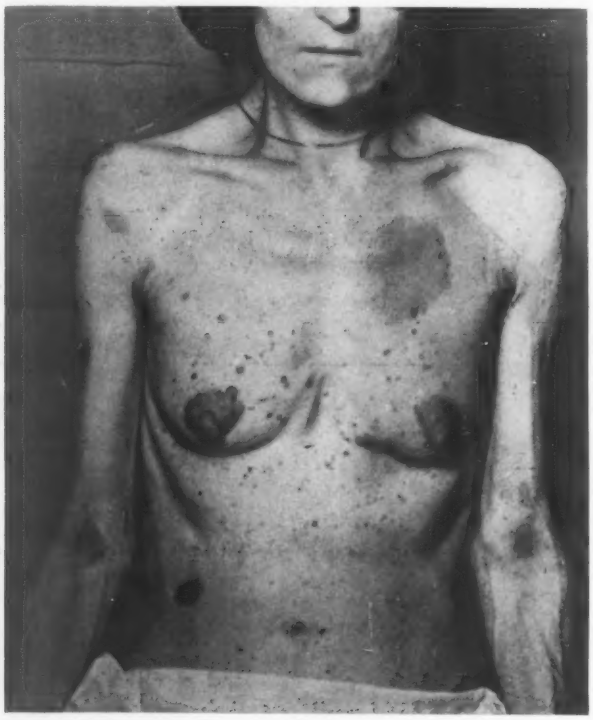

FIG. 4.—J. K. Photograph showing cafe-au-lait spots and cutaneous neurofibromata. Notice the pedunculated tumor on the right shoulder.

that she had been perfectly well until her fifth month of pregnancy (January, 1947), at which time she developed hypertension and albuminuria. This did not improve, so labor was induced in March, 1947, and a 4 lb. 7 oz. boy delivered. Several skin nodules and areas of pigmentation which had first appeared during adolescence spread rapidly and widely during the pregnancy. She also complained of constant pain in her lower left side and back during this period. After her pregnancy she noticed a large mass in her left side and a gradual loss of weight.

The patient's father died of an unknown cause, with many tumors and pigmented areas on his skin.

Physical examination. The patient appeared very cachectic. There was a large mass, grapefruit size, in the left lower quadrant of the abdomen. The skin revealed multiple, diffuse papillomas in groups and separate soft, non-tender tumors over the neck, back, chest, abdomen and legs. In addition there were many typical cafe-au-lait spots scattered diffusely over her body (Fig. 4).

Roentgenograms revealed no bony changes typical of neurofibromatosis.

Laboratory work. RBC 3,200,000; HGB 6.7 Gm. Serum calcium 10.0 mg. per 100, blood phosphorous 3.3 mg. per 100. Alkaline phosphatase 3.2 Bodansky units.

On December 14, 1947, the abdominal mass was biopsied under local anesthesia. This tumor was found to be large grapefruit size, irregularly globular, and seemed to arise in the retroperitoneal space in the left lower quadrant. Beneath its thick capsule, the neoplastic tissue was found to be necrotic and pultaceous.

FIG. 5

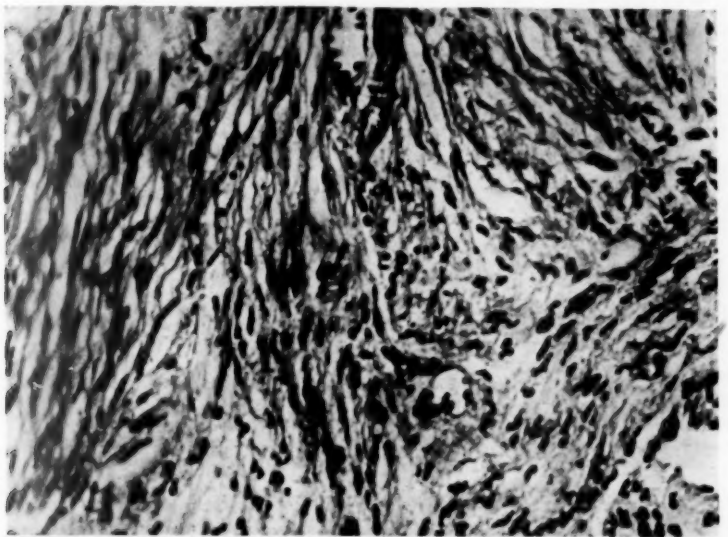

FIG. 6

FIG. 5.—J. K. This picture shows a largely fibrillar section through the tumor with variation in the size and chromatin content of the nuclei. (In other areas giant cells and rare mitotic figures were seen.) x 250.

FIG. 6.—J. M. Picture of the sciatic, tibial and common peroneal nerves showing the tumor transected. The tumor was greyish yellow with areas of necrosis and hemorrhage. Note the neurofibromata proximal and distal.

The pathologic report of the biopsy was that of a fibrosarcoma in a peripheral nerve (Fig. 5).

The patient was treated supportively with transfusions and given two courses of nitrogen mustard. The first course consisted of 4 mg. injected intravenously daily for 4 days and then repeated at the end of 2 weeks. The patient became more cachectic and the mass became larger. The patient was discharged on January 20, 1948, and expired at home on April 1, 1948.

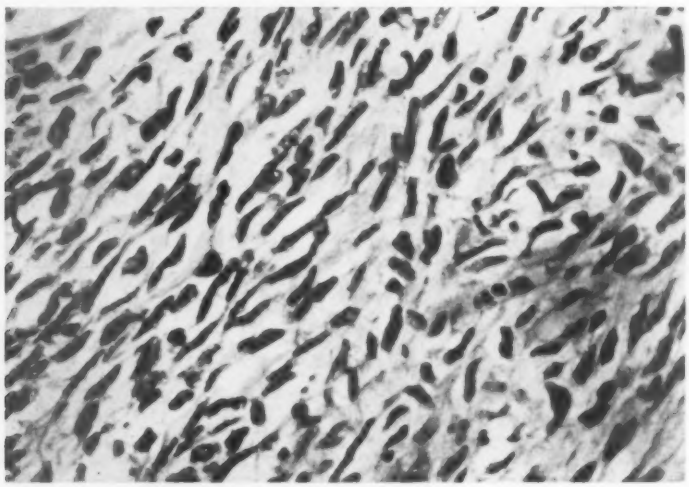

FIG. 7.—J. M. Sarcomatous area showing moderate atypism of nuclei and typical spindle cells. x 240.

Case 4. (J. M.) This 31-year-old veteran was admitted to the Surgical Service of the Marine Hospital, Buffalo, New York, on April 11, 1949. His only complaint at that time was pain in the lower left extremity, posteriorly, extending from the hip to the ankle. This had been present almost constantly since December, 1948. In January, 1949, he was treated at another hospital for thrombophlebitis of the same leg.

Family history is not reliable.

Physical examination. This patient is a rather healthy-appearing, robust young man. He has numerous tiny nodules which can be palpated subcutaneously in both upper arms. These appear to run along the course of superficial nerves. The left lower extremity displays a brownish mottling of the skin from the middle of the thigh downward. A very firm orange size mass can be palpated in the posterior aspect of the middle third of the left thigh and a softer egg size mass is present in the right popliteal space. No abnormal neurologic signs are noted. Two small cafe-au-lait spots are found, one on the lower back and the other on the left ankle.

Roentgenograms of the long bones shows no evidence of the changes found in neurofibromatosis. The chest film is not remarkable.

Laboratory work. RBC 3,891,000; HGB 75 per 100; WBC 12,500. The urinalysis and remainder of the laboratory work are non-contributory.

On May 3, 1949, the mass in the left thigh was removed and found to have its origin in the sciatic nerve. Inasmuch as the surgeon found no infiltration of the muscle, he amputated the sciatic nerve as high as possible and removed the tumor and the proximal portion of the common peroneal nerve and tibial nerve. Neurofibromata could be palpated both proximal and distal to the tumor (Fig. 6).

The pathologic report described the tumor as a "typical neurogenic sarcoma" (Fig. 7). Sections taken proximal and distal to the mass showed no evidence of cancer.

The patient has now been transferred to the Veterans Administration for further follow-up.

DISCUSSION

When neurofibromata undergo malignant change, regardless of whether they originate from ectodermal or mesodermal elements, they appear histologically and behave clinically as sarcomata. While neurogenic sarcoma may be an inaccurate title, as Trueblood[20] states, it is well established and has the advantage of creating in our minds the idea that the disease is malignant, and moreover specifies the geography of the disease, the areas and structures where such an entity might be suspected. Most of the cases of malignant transformation reported in the literature have occurred in the third, fourth and fifth decades, and have an approximately equal sex distribution.[18] The general predilection is for the deeper nerves of the extremities, but cases have been reported originating in the mediastinum, in the retroperitoneal space or in the gastro-intestinal tract.[21] Metastases are as a rule late and infrequent, occurring in 22 per cent of the patients in Hosoi's series.[18] The lungs are the most common site of the metastatic growths. There are two cases reported where lymph nodes, other than regional, were involved. In 1944 Wachstein and Wolfe[22] reported one case of sarcomatous degeneration in a patient with neurofibromatosis in which a lesion above the knee metastasized to the inguinal lymph nodes. Patients generally succumb from progressive cachexia, with pain, necrosis, infection, local disability and pulmonary metastases being contributing factors.

Biopsy or extirpation of a benign neurofibroma is not without hazard. Cases are recorded where removal of a nodule was followed shortly by the appearance of neurofibromata in other areas of the body. There are other instances reported where biopsy, incomplete removal and trauma were considered as contributing to local sarcomatous degeneration. Still other cases are known where removal of a sarcomatous growth was followed in a short period of time by malignant transformation in another neurofibroma distantly located. Simultaneous malignant transformation of neurofibromata is rare, but one case is recorded in which seven of these tumors underwent sarcomatous change.[23] These growths are prone to recur locally and repeatedly when excised.

SUMMARY

Four patients are presented who displayed clinical and microscopic evidence of multiple neurofibromatosis. Three developed sarcomata in their sciatic nerves and one developed a sarcoma retroperitoneally.

CONCLUSION

1. Patients with neurofibromata should be cautioned about the hereditary possibility of transmission of the disease and associated congenital abnormalities.

2. The diagnosis of neurofibromatosis is not difficult clinically. Biopsy of cafe-au-lait spots or neurofibromatous nodules for diagnosis should not be attempted because of the possibility of stimulating sarcomatous transformation. The lesions should be widely extirpated only if there is sudden swelling associated with pain and then the operator should be prepared to do more radical surgery if the lesion proves to be a sarcoma. Such change is especially apt to occur during periods of puberty and pregnancy.

3. Roentgen ray, radium and now nitrogen mustard have been used in the treatment of this disease with little success. Radical surgery in an early lesion is still the treatment of choice.

4. There is a wide variation in the sarcomata histologically, ranging from medullary forms to those with a more fibrillar pattern. This variation may even be noted in different sections of the same tumor.

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RECONSTRUCTION OF THE DEFORMED ARTHRITIC HAND*

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THIS IS A REPORT of a multiple surgical procedure by which a deformed arthritic hand was reconstructed into a more useful part of the extremity. Functional and cosmetic improvement was obtained and probably a foundation for preventing further increase in deformity was laid down.

CASE HISTORY

Mrs. E., a 34-year-old housewife, had had rheumatoid polyarthritis for nine years. The habitus was one frequently seen in patients suffering from this disease. Her family and past histories were not significant. The patient received most of the accepted antirheumatic treatments, including several courses of gold therapy, to which she responded fairly well. The last course of crysotherapy was given in 1946.

Examination. Examination showed a fairly well-developed white female. Her general appearance was that of a chronically ill patient. Weight: 118 pounds; height: 5 feet, 4 inches. Every joint from the temporo-mandibular joints to the ankles was involved to a greater or lesser degree. The joints most severely affected were both wrists and the periarticular and articular structures of both hands. While the lower extremities were involved, fairly good function was preserved.

Laboratory Findings. Sed. rate: 28. R.B.C.: 3,900,000. W.B.C.: 7,400. HGB 75 per cent. Serum alb.: 3.8 per cent. Serum glob.: 2.9 per cent. Serum calc.: 10.5 mgr. per cent. Alk. phosphatase: 3.9 Bodansky units. Serum phosph.: 3.6 mgr. per 100. Blood uric acid: 3.1 mgr. per 100.

Right hand. This showed extensive atrophy of the interossei. No ulnar deviation of the fingers was noticed. The thumb was markedly deformed; the distal phalanx was in the position of extreme hyperextension due to subluxation, and so was the proximal phalanx. There was a painful limitation in the motion of the metacarpophalangeal joints; each had a different range, the fourth and fifth being the most painful. Each proximal phalanx was subluxated under the head of the respective metacarpal bone. There was an average of 20 degrees of flexion contracture in the metacarpophalangeal joints; active flexion from that point was possible to 35 degrees. The patient was not able to make a fist (Fig. 1).

Index finger. The proximal interphalangeal joint was rigid in slight hyperextension. The distal interphalangeal joint could be actively flexed from its normal extended position approximately 15 degrees.

Midfinger. The proximal interphalangeal joint was in about 15 degrees of hyperextension with no active or passive flexion in this joint. The distal interphalangeal joint was not in flexion contracture but rather in the position of 10 degrees of flexion from which passive extension was full and active flexion restricted.

Fourth and fifth fingers. Changes in the fourth and fifth fingers were restricted mostly to the metacarpophalangeal joints with extensive subluxation and a considerable amount of pain in these joints. The deformity in the other finger joints of the fourth and fifth fingers was only moderate.

* Submitted for publication September, 1948.

OPERATION

The reconstruction operation was performed in two stages. The thumb was operated upon in the first stage and the other fingers were done in the second stage.

Thumb. A pneumatic tourniquet was used. On February 2, under general anesthesia (ether) through a midlateral incision, the proximal and distal joints of the thumb were exposed. The articular surfaces of the respective phalanges were found to be in an extreme degree of subluxation and their articular cartilage destroyed much more extensively than one could anticipate clinically and roentgenologically. The periarticular structure as well as the synovium of the smaller joints was found to be thickened and inflamed. When the joint capsule was incised a scant amount of grayish white creamy

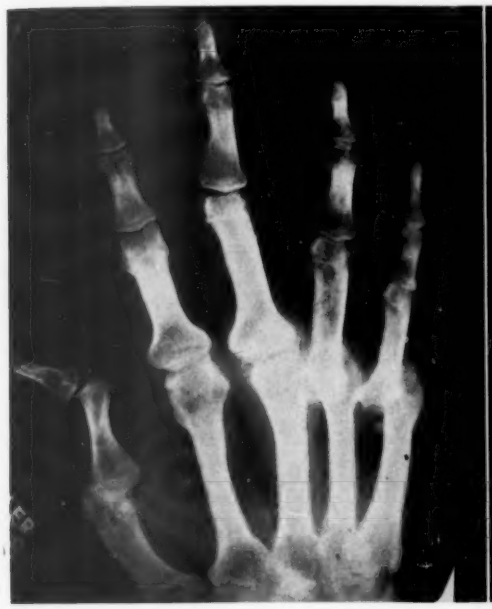

FIG. 1

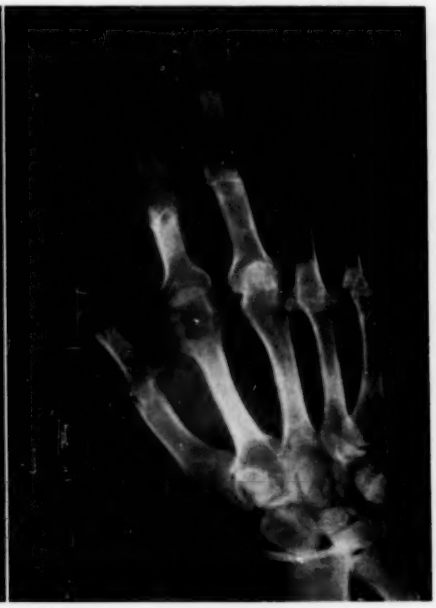

FIG. 2

FIG. 1.—Preoperative x-ray of right hand showing subluxation of proximal and distal joints of thumb. It also indicates subluxations of the metacarpophalangeal joints increasing in degree from the index to the fifth fingers.

FIG. 2.—X-ray following fusion of metacarpophalangeal joint of the thumb. The proximal phalanx was shortened in order to correct subluxation in the distal joint. The subluxation of the metacarpophalangeal joints is readily seen.

substance escaped from each joint. There was no motion in the distal joint. In order to reduce the proximal phalanx which was subluxated in toto it was necessary to dissect it out completely, stripping it of all its soft tissue structures. About ⅛ inch of the proximal portion of this phalanx was resected with an electric saw and the same amount was removed from the head of the first metacarpal. Then the head portion of the metacarpal was beveled and the entire first phalanx was shifted proximally (Fig. 2). The intention was to obtain a fusion at the metacarpophalangeal joint of the thumb in a corrected position. Closure was obtained in layers and the thumb was immobilized in a dorsolateral plaster-of-paris splint. Primary healing was obtained. Following the removal of the sutures, superficial skin necrosis developed in a small area with no ill effects whatever. In three weeks clinical fusion was obtained.

Second stage. Three weeks after the first operation the following procedures were performed in one stage. A pneumatic tourniquet was applied to the right arm. Under general anesthesia the four metacarpophalangeal joints were exposed through a slightly curved transverse incision from the metacarpophalangeal joint of the index finger to the same joint of the little finger (Fig. 3). A layer by layer dissection was carried out. Specimens were removed of every tissue including the interosseus and lumbricales muscles. Each cartilaginous member participating in the joints was dissected out and inspected. The proximal phalanges were found to be increasingly subluxated from index to fifth finger. The metacarpal heads of the index and midfinger were found to be intact, those of the fourth and fifth almost completely destroyed. A few drill holes were made with a motor drill in the section of the metacarpal head of the index finger where the cartilage

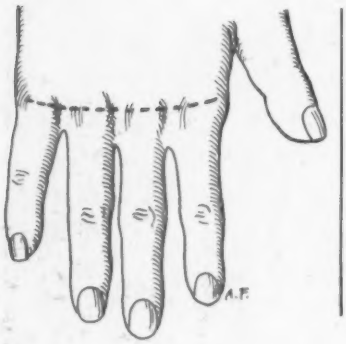

FIG. 3

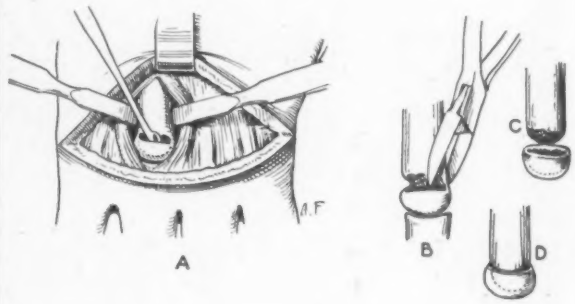

FIG. 4

FIG. 3.—Showing skin incision.
FIG. 4.—Demonstrating the operative procedure.

meets the cortex and about ¼ inch proximal to this line. The opening thus created was entered with a curette and the head of the metacarpal bone was carefully scooped out so that a bony layer of ⅛ inch remained attached to the cartilaginous cup. This procedure was done through the dorsal cortex of the metacarpal bone. The two lateral cortices and the anterior cortex were removed with a bone cutting scissors. The cartilaginous cup and the thin layer of bone were detached from the rest of the bone. Soft tissue attachments were severed sufficiently to shift the cartilaginous cup proximally. Depending upon individual requirement the shortening of the gap produced may vary from ⅛ inch to ⅜ inch. The metacarpal shaft was reshaped to receive the cartilaginous cup and the cup was reapplied on the shaft. No internal fixation was used (Fig. 4a, b, c). The same procedure was carried out with the mid-finger. The metacarpal heads of the fourth and fifth fingers were excised by the technic which was described by the author previously.[1] Closure was done layer by layer. The hand was put on a molded plaster-of-paris splint, holding the fingers in a moderately flexed position and the metacarpophalangeal joints in about 20 degrees of flexion.

After this operative procedure it was found that the proximal interphalangeal joint of the index finger, previously fixed in extension, could be flexed with relative ease as compared with the motion when the patient was under anesthesia before the operation started. The hyperextended proximal interphalangeal joint of the mid-finger, however, could not be flexed after the same procedure was carried out at the metacarpophalangeal joint of this finger. For this reason the procedure performed upon the second and third metacarpal heads was carried out on the head of the proximal phalanx (Fig. 5).

Postoperative care. An anterior plaster-of-paris splint was used for the thumb, holding the thumb in functional position for three weeks. After the second procedure the hand was immobilized for two weeks on an anterior plaster-of-paris splint holding the proximal finger joints in extension. After two weeks, another splint was applied with the proximal finger joints in 45 degrees of flexion. Active exercises began three weeks after operation. The splint was removed four weeks after the operation and intensive physiotherapy started.

FOLLOW-UP

A period of 14 months shows the following changes as compared with the preoperative findings.

FIG. 5

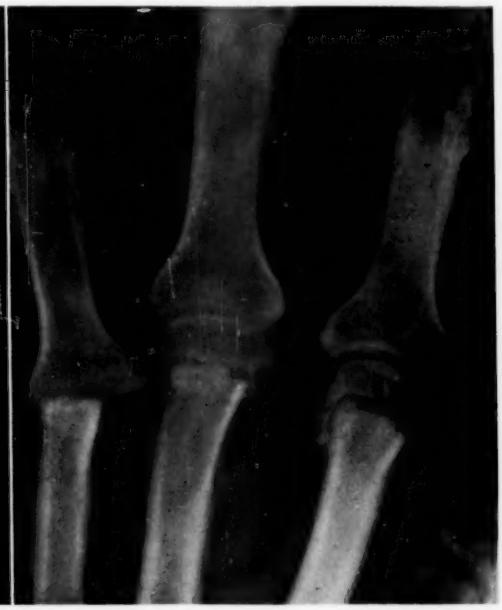

FIG. 6

FIG. 5.—Showing middle finger joint of third finger. The distal portion of the proximal phalanx was shortened in the fashion described for the metacarpal heads in order to correct the hyperextension deformity and improve joint motion.

FIG. 6.—X-ray 4½ months postoperatively demonstrating proximal finger joints of index and midfinger. The shifted metacarpal heads are in good position. There is no subluxation in these joints. There is still some degree of subluxation in the proximal interphalangeal joints of the fourth and fifth fingers.

Right thumb. Subluxation of the distal phalanx was corrected as well as that of the proximal phalanx. There was solid fusion of the first metacarpophalangeal joint. There is 20 degrees of active flexion in the interphalangeal joint of the thumb. There is complete functional use of the thumb otherwise.

Index finger. There is no subluxation in the metacarpophalangeal joint. Active extension is possible to 175 degrees. Passive extension is to 180 degrees. Active flexion is to 100 degrees. The proximal interphalangeal joint is in a position of 180 degrees from which it is possible to flex it actively to 160 degrees and passively to 140 degrees. In the distal interphalangeal joint there is active flexion to 160 degrees and passively it can be increased by another 5 degrees.

Midfinger. The subluxation of the metacarpophalangeal joint has been corrected. Active extension is to 175 degrees and passive extension is to 180 degrees. Active flexion is possible to about 100 degrees. The previously hyperextended proximal interphalangeal joint is in an attitude of 170 degrees of flexion from which it is not possible actively or passively to extend it. There is 20 degrees flexion in this finger joint. The position of the distal interphalangeal joint is unchanged but there is about 15 degrees increase in active flexion (Figs. 6 and 7).

The fourth and fifth metacarpophalangeal joints are in about 175 degrees of extension. Active flexion is possible to about 95 degrees, passively this can be increased another 5 degrees. There is still some degree of subluxation in these joints as seen in the roentgen ray film.

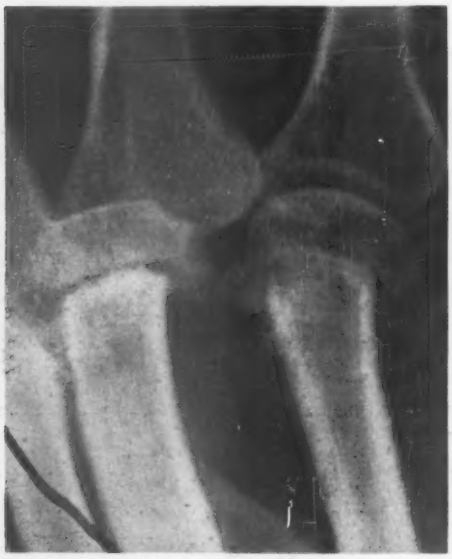

FIG. 7.—Oblique view of proximal finger joint of index and midfinger.

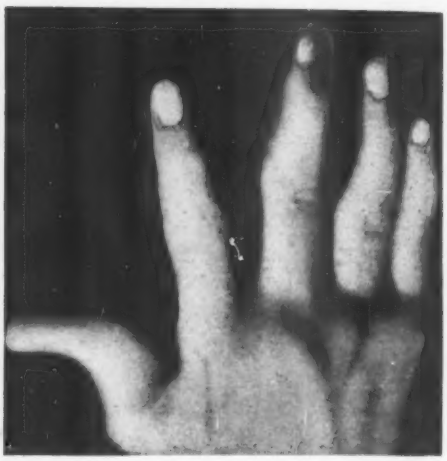

FIG. 8.—Preoperative photograph of hand.

If we compare the present status of this hand with the preoperative one there is definite improvement in active function and in the physiological position of the fingers. The most evident improvement is in the general appearance of the hand (Figs. 8, 9 and 10).

DISCUSSION

It has been the author's experience that surgical procedures, if used judiciously, have excellent possibilities in rendering a painful arthritic hand lastingly free of pain. At the same time, function may be improved to an extent not experienced with other methods. Excision of the metacarpal heads as reported[1] has given very satisfactory results.

The excision of the metacarpal heads in the treatment of rheumatoid arthritis was performed in 11 cases to date. Two cases have been followed for four years and eight months; five cases were followed for three years; two cases for one year and a half, one case for 14 months and one case for ten months. In each case the existing pain was completely eliminated and has not returned. Function was improved in every case in varying degrees. In gen-

eral there was about 8 to 15° loss of active extension and about 25 to 55° gain in active flexion as compared with the preoperative function. There was no case which resulted in instability or functional impairment.

The prompt elimination of pain was the striking impression gained from the first cases. Active motion was only moderately improved in the early stages. The reason for this was the demonstrated imbalance between the intrinsic and extrinsic muscles which was already present due to pathologic conditions in the muscle,[2] and which was further disturbed by the excision of the metacarpal heads. However, as time went on function improved in every case.

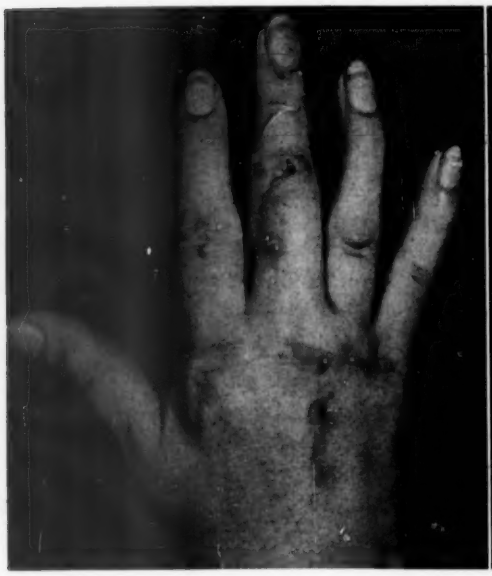

FIG. 9

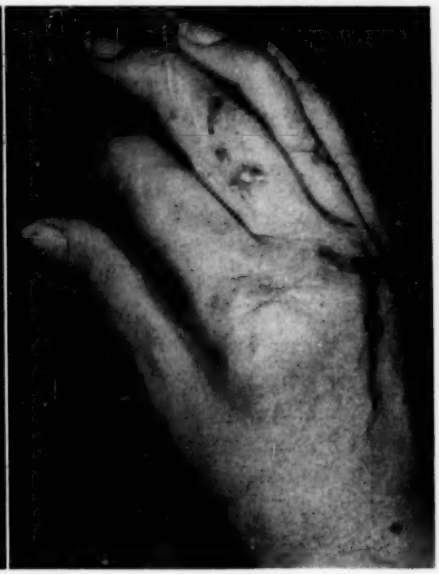

FIG. 10

FIG. 9.—Postoperative photograph of same hand.
FIG. 10.—Another view of the same hand showing the corrected hyperextension deformity of middle finger joint of midfinger.

In performing this operation in different stages of the disease it was found that the less advanced the pathologic changes, the better the functional result. It was our experience that the more recently involved joints had a better functional recovery than joints operated upon when pathologic changes in tissues and joint obstruction were more advanced.

No claim is made, however, that these procedures will restore an arthritic hand to its full functional use. The intrinsic muscle apparatus of the hand is too extensively involved by the rheumatoid process to expect complete recovery by surgical means.[2, 3] However, the procedures improved the function of the hand that was previously crippled by rheumatoid arthritis. A last-

ing improvement was obtained with the excision of the metacarpal heads, as shown in a limited number of cases followed for almost five years.

It is too early to draw final conclusions as to the shifting of the cartilaginous cups. So far the result is satisfactory. The possibility of asceptic necrosis, while considered to be remote, is vividly kept in mind. Shifting of the cartilaginous cups appears to be preferable to the excision of the metacarpal heads in that it permits more stability at the metacarpophalangeal joints. The cartilage is preserved, which is an advantage for the joint so created. The contour of the metacarpal heads is preserved in part and thereby gives a better appearance. The author considers this type of operation more applicable to the younger age group, if the cartilage is intact. The excision of the metacarpal heads may be reserved for the aged arthritic patients and for those cases where the cartilage has been destroyed.

CONCLUSION

1. A procedure is presented by which a hand seriously deformed and extremely painful due to rheumatoid arthritis was satisfactorily reconstructed.

2. A deformed functionally impaired thumb was reconstructed by complete dissection and shortening of the proximal phalanx. Fusion of the metacarpophalangeal joint was obtained and the distal phalanx could be reduced into its normal position. Useful active function could be maintained in this interphalangeal joint. The patient has been followed for 14 months.

3. A case is reported in which proximal shifting of the metacarpal heads was performed on the second and third metacarpal bones of the right hand. Functional and cosmetic improvement was obtained and maintained for a period of 14 months.

4. The merits of the two procedures—one which removed the metacarpal heads and the other which shifted the cartilaginous cups—are weighed and discussed.

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GALLSTONE INTESTINAL OBSTRUCTION*

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GALLSTONE AS A CAUSE for intestinal obstruction is uncommon but not rare. The first recorded case was by Bartholin in 1654. In 1914 Wayne compiled 334 cases from the literature. Walters and Snell[1] in 1940 stated that 2 per cent of all obstructions of the bowel are due to gallstones and Foss and Summers[2] in 1942 stated that gallstone ileus occurred in 0.3 per cent of their cases of diseases of the gallbladder and bile ducts. In 1943 Hand and Gilmore[3] reported that in 12,153 cases of intestinal obstruction collected from the literature, gallstones were responsible in 208 instances, or 1.7 per cent.

It happened that on the Fourth Surgical Division of Bellevue Hospital from 1928 to 1948, there was no case of gallstone ileus while at St. Vincent's Hospital from 1936 to 1949 there were ten cases, six occurring in 1948.

As to age of patients: Since gallstone intestinal obstruction is secondary to biliary lithiasis, which is more frequent in persons past 40 years of age, the fact that the condition occurs most commonly in individuals over 40 is not unexpected. Wortman, quoted by Wangensteen[4] in 1942, reported a case in a female of 25 and stated that this is the youngest age at which this type of bowel obstruction has been observed. Authors agree that the usual age is over 60. In our ten cases the average was 64, the youngest being 48 and the oldest 81.

As to sex: Gallstones are about four times as common in females as in males, according to Carter, Greene, and Twiss,[5] and gallstone ileus is likewise more common in females. Nine of our ten cases occurred in females and one in a male.

Pathogenesis. Gallstones originate in the biliary tract and almost always in the gallbladder. The calculus enters the gastro-intestinal tract almost always via the gallbladder, although stones have been reported as passing through the papilla of Vater. In the latter case it is probable that the calculus increased in size in the intestine or caused obstruction by intestinal spasm. It is possible for a gallstone to ulcerate through the common duct into the intestine.

The stone usually enters the gastro-intestinal tract by way of the first or second portion of the duodenum but may enter the stomach or colon directly. Wakefield, Vickers, and Walters,[6] in a review of 152 cases of nonsurgical cholecystenteric fistulas at the Mayo Clinic, found 101 between the gallbladder and duodenum, 33 between the gallbladder and colon, seven

* Submitted for publication April, 1949.

between the gallbladder and stomach, and 11 between the gallbladder and multiple adjacent organs and intestine. In only about ten per cent of these cholecystenteric fistulas did gallstone ileus occur.

The usual sequence of events is cholelithiasis, acute cholecystitis, gangrene and perforation of the gallbladder against the duodenum and pressure necrosis of the gallstone into the duodenum. The formation of the fistula and discharge of the gallstone presumably takes at least several days.

The gallstone may remain protruding into the duodenum, as was the case recently reported verbally to us from Gouverneur Hospital; the calculus may remain incarcerated in the duodenum as in one of our patients, or it may pass into the stomach and be vomited. Usually, however, the stone passes distally.

There may be multiple calculi. From the fact that there are about ten times as many nonsurgical cholecystenteric fistulas as there are operations for gallstone ileus, one readily deduces that most gallstones pass through the entire intestine and out of the rectum with no, or minimal, symptoms. It is thought that 2.5 cm. is the critical size of a stone to cause obstruction. A calculus of this size may cause obstruction by inducing intestinal spasm. A round stone is more apt to cause trouble than an oval stone of the same size, and an irregular stone is more apt to become caught in the mucosa.

The pathology is usually a simple mechanical block to which may be added the complication of perforation and suppurative peritonitis. Intestinal spasm doubtless plays an important part, the tendency of the intestine being to grab a calculus and force it distally, as occurs to the inflated balloon of a Miller-Abbott tube. Intestinal spasm may complete the obstruction; this occurred in two of our cases where the stone was obstructing jejunum in one case and upper ileum in one case. Were it not for the spasm, intestinal contents might well by-pass the calculus. Occasionally, according to Wangensteen,[4] the obstruction partakes of the nature of a volvulus due to the fact that the increased weight caused by the accumulation of fluid and gas above the point of obstruction may cause torsion in the loop. Perforation may occur above the site of the gallstone, as in our case 4, due to extreme dilatation of the intestine proximal to the block.

Mayo[7] states that the history of chronic cholecystitis is of little value in diagnosis inasmuch as a patient, especially an elderly one, may have an intestinal obstruction and a chronic cholecystitis not related to the obstruction. Only two of our ten cases gave a history of chronic cholecystitis.

The symptoms and signs vary according to several factors, the chief being the size of the stone and the site of obstruction. Probably most calculi pass without causing serious trouble. The caliber of the small intestine decreases progressively distally and the ileocecal junction is the narrowest. These anatomic facts account for the finding at operation of the majority of the calculi in the ileum near the ileocecal region. Retroperistalsis may move a stone proximally.

No doubt the necessary acute cholecystitis preceding the formation of the fistula causes symptoms, but it has been difficult for us to elicit this in our histories.

A stone impacted in the first part of the duodenum gives the usual symptoms and signs of any obstruction at that site, as in our case 10.

TABLE I.—*Incidence of Various Types of Organic Obstruction (Based on Vick's 6,892 Cases)**

Simple Obstructions	No. of Cases	Percentage of Total	Strangulations	No. of Cases	Percentage of Total
1. Intussusception	1034	15.0	1. Strangulated inguinal hernia	1378	20.0
2. Carcinoma	895	13.0	2. Strangulated femoral hernia	1348	19.5
3. Adhesions	505	7.35	3. Strangulated umbilical hernia	371	5.4
4. Gallstones	47	0.7	4. Other hernias	170	2.5
5. Congenital atresias, etc.	40	0.6	5. Internal strangulation	790	11.4
6. External compression	29	0.4	6. Volvulus	176	2.6
7. Stricture	36	0.5	7. Embolism and thrombosis	49	0.7
Total	2,586	37.6	Total	4,282	62.1

* Adapted from Maingot, Rodney: Abdominal Operations, p. 1092, New York, 1940. D. Appleton-Century Company, Inc.

A calculus causing partial or complete small intestinal obstruction gives the cardinal symptoms and signs of any acute small intestinal obstruction, namely pain, vomiting, and abdominal distention. The pain is periumbilical, colicky, lasting usually one to two minutes and recurring every few minutes. These findings were present in all of our first nine cases. Abdominal

TABLE II.—*Location of Gallstone in Intestine*

Duodenum	1	Upper ileum	1
Jejunum	2	Lower ileum	6

tenderness was noted in six cases, obesity in four, and a mass in no case. Lack of bowel movement may or may not be significant.

None of our cases had clinical jaundice despite the presence of a cholecystoduodenostomy and acute intestinal obstruction.

Diagnosis. Surgeons agree that the diagnosis is seldom made preoperatively. Except for remittance in some cases, the symptoms and signs of the intestinal obstruction are no different from obstruction due to adhesions.

The roentgenologist gives us our greatest help. Rigler, Borman and Noble[8] studied 14 gallstone obstruction cases and found that roentgen ray examination alone could have made the diagnosis in 13. Nitkin and Lesser[9] in 1943 stated that, of 36 cases reported in the literature in which roentgenologic examination was made prior to operation, 22 revealed visualization of the biliary radicles recognized only after correlation with the operative findings.

The roentgen ray criteria are well established,[8] namely:

1. Air or contrast medium in the biliary tract.

2. Direct visualization of the gallstone or indirect visualization by means of contrast medium in the intestine.

3. Change of position of a previously observed stone, *e.g.*, a gallstone formerly identified in the gallbladder, found absent from the gallbladder and in the intestinal region.

TABLE III.—*Duration of Symptoms Until Hospital Admission*

Case	Days	Case	Days
1	7	6	3
2	3	7	14
3	14	8	3
4	2	9	1
5	7	10	30

4. Evidences of partial or complete intestinal obstruction.

Rigler *et al.* state that roentgenograms taken over the right upper quadrant in the antero-posterior and postero-anterior projections are of greater value than films centered over the mid-abdomen.

As for roentgen ray evidence in our cases: Diagnosis was established preoperatively in one case, namely Case 10, where a calculus was visualized

TABLE IV.—*Mortality of the Main Types of Acute Intestinal Obstruction**

Disease	Approximate Mortality Per Cent
Gallstone obturation	50–60
Carcinoma of the colon	35–40
Adhesions	30–35
Internal strangulation	30–35
Volvulus	50–55
Intussusception	15–20
Strangulated inguinal hernia	10–15
Strangulated femoral hernia	15–20
Strangulated umbilical hernia	30–40

* According to Maingot, Rodney: Abdominal Operations, p. 1093. New York, 1940. D. Appleton-Century Co., Inc.

in the duodenum and barium seen in the biliary tree. Diagnosis was not made by roentgenogram preoperatively in any of the nine cases of small intestinal obstruction but might have been in Cases 1, 3, and 5, where a calcified mass was visualized and later proved to be a gallstone. In no case did a review of the roentgen ray films taken preoperatively show gas in the biliary tree.

Only one of our nine cases of intestinal obstruction had a preoperative diagnostic impression of gallstone ileus. The presumptive diagnosis was made by the referring internist, who had sent in a similar case a few weeks previously, with the agreement of the surgeon.

However, the preoperative diagnosis as to acute small intestinal obstruction was correct in eight of the nine cases, one being preoperatively considered acute appendicitis.

Operation is indicated urgently but not emergently. The danger of perforation and peritonitis is considerable, but should not make the surgeon overlook the need for preoperative preparation of the patient, especially as to hydration and electrolyte balance. Each case should be individualized and no hard and fast rule should be laid down. In most cases 24 to 48 hours preparation should be sufficient. Prolonged treatment with intestinal intubation and suction is generally unwise. Abdominal tenderness and a high white cell and/or differential count increase the indication for early laparotomy.

Operative procedure. Gallstones in the intestine are difficult to crush and it is unwise to attempt to do so.[4] Usually the gallstone cannot easily be pushed distally into unobstructed bowel and it is wiser if possible to milk the stone proximally for removal, because there may be an ulceration of the intestine at the site of lodgement of the calculus. Otherwise, it must be removed in situ. Most surgeons use a longitudinal incision, closed transversely; others prefer a transverse incision. Spillage of intestinal contents should be minimized. Resection of bowel is seldom necessary. Ileostomy is usually not indicated. Search for multiple stones may be indicated especially if a facetted stone is found. The cholecystoduodenal fistula should not be operated upon at the time of removal of the intestinal calculus and probably not at a later date. Our follow-up shows no instance of symptoms from the cholecystoduodenal fistula.

Small intestinal obstruction is a lethal disease and gallstone, as a cause, one of the most lethal. The factors causing the high mortality are largely beyond the physician's control, namely: (1) The age of the patients, usually in their sixties and in our series averaging 64; (2) cardiovascular-renal disease, and (3) the delay in the patient reaching a hospital—in our series an average delay of six days.

The reduction in mortality in recent years is probably due to several factors, including (1) better roentgen ray diagnosis, (2) better preoperative preparation, (3) better anesthesia, (4) better postoperative care, (5) the greater use of whole blood, and (6) chemotherapy.

The mortality in our ten cases was 40 per cent. The postoperative mortality was 33⅓ per cent, one patient dying without operation. Of the six cases in 1948, five lived and one died, a mortality of 16⅔ per cent.

Causes of Death. (1) Two of toxic ileus, one of which came to autopsy. (2) One of perforation of jejunum and acute suppurative peritonitis, not operated upon, but confirmed at autopsy. (3) One of acute pyelonephritis and uremia.

CASE REPORTS

Case 1.—A. L. was a 63-year-old female admitted on August 19, 1939, complaining of collicky periumbilical pain and persistent vomiting of 4 days' duration and with a temperature of 104° F. and a pulse of 120.

Her past history was irrelevant.

Her present illness began two weeks prior to admission with an attack of severe right upper quadrant pain radiating to the right back and accompanied by vomiting. These symptoms were intermittent with several days of comparative ease.

Physical examination showed a very ill patient with the abdomen distended and with no mass, no tenderness and no rigidity.

Scout roentgen ray films showed marked gaseous distention of the small intestine and fluid levels. There was also a calcified mass in the left pelvic fossa below the level of the distended coils of the intestine.

Laboratory examinations showed Hg. 94 per cent, RBC 5M, WBC 7,160 with 86 per cent polymorphonuclear cells. The urine was normal.

Course. The abdominal distention was relieved by the use of a Miller-Abbott tube and suction and intravenous fluids were given. The attending surgeon, Dr. C. Howley, rated her as a fair risk and laparotomy was performed on the day of hospital admission. The small intestine was found to be distended about 18 inches above the ileocecal junction at the site of a hard irregular foreign body which was flanged at the ends like a spool. There was no injury to the bowel. The foreign body could not be moved, so an enterotomy was done through a transverse incision at the site, the gallstone removed, and the intestine repaired. The patient died 24 hours later. Autopsy revealed a non-surgical cholecystoduodenostomy and a toxic ileus.

Two weeks prior to hospital admission the patient had had an acute cholecystitis followed by passage of the gallstone into the intestine.

Case 2.—M. B. was a 65-year-old white female, admitted with a 3-day history of pain in the right lower quadrant associated with vomiting and abdominal distention. Scout roentgen ray films showed gaseous distention of the small intestine with fluid levels.

Laparotomy was done on the day of admission. The entire small bowel was found distended to 3 times normal size down to a point 1½ feet from the ileocecal valve. At this point a foreign body, the size of a golf ball, was seen. The gallstone was removed through an enterotomy. A fistula found connecting the gallbladder and duodenum was excised, the opening in the duodenum closed, and a cholecystectomy done.

The postoperative course was one of progressive decline and she died on the third postoperative day. No autopsy was done.

Case 3.—M. S. was a 61-year-old female, admitted on December 8, 1942, with a history of cramplike abdominal pain of two weeks' duration associated with failure to move the bowels for five days and vomiting for two days. The pain was intermittent and very severe.

Physical examination of the abdomen revealed a large right rectus hernia at the site of appendectomy 12 years previously.

Scout roentgen ray film examination of the abdomen was essentially normal except for an oval-shaped calcified body in the right pelvic fossa in the line of the right ureter.

Urinalysis was normal and blood Kahn negative.

Laparotomy was performed four days after admission. In the hernial sac was found collapsed gut and a 4.5 cm. by 3 cm. gallstone which had occluded the lumen of the ileum. Enterotomy and herniaplasty were done.

Thirteen days postoperatively a fecal fistula developed. Eighty-eight days postoperatively she was operated upon for an abdominal wall sinus. She was discharged from the hospital on the one hundred and seventh postoperative day with the wound clean and healing slowly.

Case 4.—M. F. was a 76-year-old white female, admitted to the hospital December 28, 1944, complaining of nausea and vomiting of two days' duration. The pain was at first generalized and then localized to both lower quadrants. There was no fever and

there had been no bowel movement for 48 hours. The abdomen was distended and tympanitic, with no mass and no rebound tenderness. There had been no previous similar episodes.

Scout roentgen ray films of the abdomen showed a moderate collection of gas in the small intestine and no fluid levels.

Laboratory. Hg. 85 per cent; RBC 5.2 M; WBC 26,900 with 84 per cent polymorphonuclears. The urine was normal; the blood sugar 112; the urea nitrogen 29; and the blood Kahn negative.

Course. The patient's treatment included intravenous fluids and intestinal intubation with suction. Her course was acutely downhill and she died on January 6, 1945.

Autopsy findings. Generalized acute suppurative peritonitis; spontaneous perforation of the jejunum two feet from the duodenal-jejunal junction; an oval, rough gallstone measuring 3.5 cm. by 2 cm. six feet from the duodenal-jejunal junction; a wide-mouthed fistula between the neck of the gallbladder and the duodenum; several faceted stones 1.5 cm. in diameter in the lumen of the dilated neck of the gallbladder.

FIG. 1.—Gallstones removed from Cases 5, 6, 8.

Case 5.—E. T. was a 50-year-old markedly obese female admitted to the hospital on December 29, 1947, in a moribund condition. She vomited fecal-smelling brownish red fluid in large quantities several times while being examined. Pulse and blood pressure were not obtainable. She improved with supportive treatment, including intravenous fluids, plasma, and blood, and Levin tube gastric intubation with suction.

History revealed that she had been ill at home for one week and had been vomiting most of that time. She had had no abdominal operation.

Physical examination of the abdomen revealed marked gaseous distention, no tenderness, and no mass.

Small intestinal obstruction was diagnosed and it was felt that emergency operation would be fatal to the patient.

The following day her condition had improved. On January 2, 1948, scout roentgen ray films of the abdomen showed much gaseous distention of the jejunum and ileum with no fluid levels. On January 4, 1948, a Miller-Abbott tube was passed and roentgenograms taken on January 6, 1848, showed the tube in the jejunum. History and cooperation were difficult to obtain owing to the low mentality of the patient.

On January 6, 1948, the total blood serum proteins were 4.4; the hemoglobin 90 per cent; RBC 4.3 M; she had a normal bowel movement. The next day no change in

condition was noted. On January 8, 1948, the blood serum albumen was 3.8; globulin 2.25; urea nitrogen 48; carbon dioxide combining power of the blood 59; blood chlorides 320.

On January 9, 1948, laparotomy was performed by us. A foreign body was quickly palpable in the jejunum and was removed through a vertical enterotomy, the incision being closed transversely. The gallstone was 4 cm. by 2.5 cm. and oval in shape. Palpation revealed an apparently inflammatory mass in the region of the gallbladder and duodenum and the presumptive diagnosis of a spontaneous cholecystoduodenal fistula was made.

Postoperatively after a stormy first day or two she made steady progress. On the fifth postoperative day intestinal intubation was discontinued. On January 15, 1948, urea nitrogen was 6. On the tenth day an abdominal wound infection was found and all sutures were removed and the wound laid open. Chemotherapy was discontinued on the eleventh postoperative day.

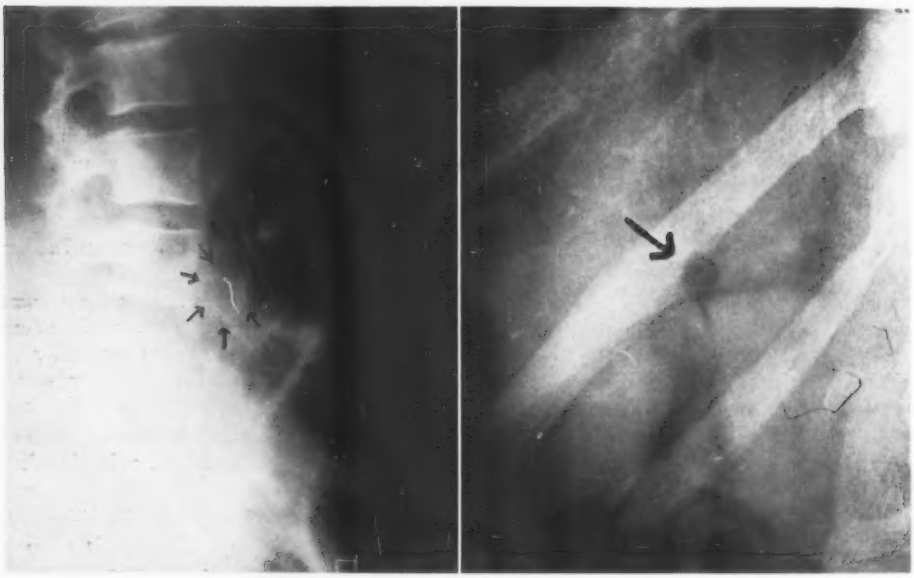

FIG. 2 FIG. 3

FIG. 2.—Preoperative scout roentgenogram of abdomen in Case 5 showing gallstone in intestine, not recognized until after operation.

FIG. 3.—Roentgenogram of abdomen in Case 6 taken postoperatively and showing gas in biliary tree.

She was discharged from the hospital on the fifty-sixth postoperative day with a granulating wound. She has developed a postoperative incisional hernia but otherwise is well.

Case 6.—D. R. was a 48-year-old male, admitted to the hospital on January 10, 1948, complaining of periumbilical pain and vomiting of three days' duration. The pain was intermittent and did not radiate. The vomitus was gastric contents. There had been no bowel movement for three days.

Physical examination of the abdomen revealed marked gaseous distention. No mass was palpable and there was no rigidity.

Roentgenograms of the abdomen in the prone and erect positions showed gaseous distention and fluid levels in the small intestine, probably the result of mechanical ileus.

Laboratory data. WBC were 15,500 with 82 per cent polymorphonuclears; urea nitrogen 22 mg. per cent; total proteins 6.4; blood Kahn negative; urine showed albumen 1 plus, sugar 3 plus.

The patient was hydrated parenterally and operated upon seven hours after admission by Dr J. Bruckner. The small intestine was found moderately distended and a gallstone the size of a walnut was removed by longitudinal enterotomy 6 inches proximal to the ileocecal valve. There was no ulceration of the intestine at the site of the calculus.

The patient did well. A gallbladder roentgen ray series with dye did not visualize the gallbladder. However, a small but persistent gas bubble was noted in the right upper quadrant in the location of the gallbladder. He was discharged from the hospital on the eleventh postoperative day and has remained well.

Case 7.—T. F. was a 60-year-old female admitted to the hospital on January 22, 1948. She had been ill at home for two weeks with intermittent abdominal pain and vomiting, thought to be due to mushroom poisoning. Dr. J. DiFiore diagnosed acute small intestinal obstruction and referred her for operation. She had had no previous abdominal operation.

Physical examination of the abdomen revealed gaseous distention, tenderness, rigidity, and no mass.

Scout roentgen ray showed gaseous distention and fluid levels in the small intestine.

Laboratory data. WBC 17,600 with 83 per cent polymorphonuclears; urine had a specific gravity of 1.004 and many clumps of pus cells.

The patient was hydrated and a Levin tube and suction used.

The diagnostic impression was acute small intestinal obstruction and the possibility of a gallstone obstruction was considered.

Laparotomy was done on the day of admission and the entire small intestine was found to be markedly distended down to 6 inches from the ileocecal junction where obstruction was caused by a gallstone the size of two walnuts. Palpation revealed what was presumably a cholecystoduodenal fistula. Enterotomy was performed by longitudinal incision, closed transversely.

Postoperative course. The patient did well as far as the intestinal obstruction was concerned and on the fourth day was put on a soft diet. On the seventh day her urinary output diminished and urinalysis showed many white blood cells. On the ninth day the blood urea nitrogen was 165 and creatinine 5.4. Despite medical treatment she died on the thirteenth postoperative day of pyelonephritis and uremia, the intestinal obstruction having been cured. No autopsy was done.

Case 8.—E. L. was an 81-year-old female who was admitted to the hospital with a three-day history of pain, vomiting, abdominal distention, and absence of bowel movement. She was referred by Dr. J. A. DiFiore with a diagnostic impression of acute small intestinal obstruction, possibly due to a gallstone.

Her past history included a gallbladder attack 20 years prior. There had been no abdominal operation.

Physical examination of the chest revealed emphysematous breathing. There was minimal cardiac enlargement, and a systolic apical murmur. Regular rhythm was present. Blood pressure was 156/80. The abdomen was greatly distended and tympanitic. There was tenderness throughout. Roentgenograms of the abdomen were not completely satisfactory but showed gaseous distention of the jejunum. Hg. 100 per cent; RBC 4.93 M; WBC 12,550; polymorphonuclears 64 per cent, lymphocytes 32 per cent, monocytes 3 per cent; urea nitrogen 19; chlorides 585; urine showed a 1 plus albumen. There were many red blood cells, white blood cells, hyaline and granular casts. The preoperative impression was acute intestinal obstruction (gallstone ileus).

Exploratory laparotomy was done with removal of a gallstone from the terminal ileum. On the second postoperative day, she developed signs of congestive failure.

Postoperative atelectasis with secondary pneumonitis was also found. She responded to therapy. Her fluid balance was carefully watched. Postoperatively, her urea nitrogen was 34, but dropped to 26 on the seventh postoperative day. She was discharged on the twenty-fourth postoperative day in very good condition. She has remained essentially well.

Case 9.—A. A. was a 65-year-old white female admitted on July 20, 1948, with a chief complaint of cramplike periumbilical pain of ten hours' duration.

Her past history was significant in that she had been treated for indigestion, and on June 7, 1948, had been admitted by ambulance with a chief complaint of upper abdominal pain of one day's duration. The pain had been severe and intermittent. She had improved after administration of phenobarbitol and belladonna and had been discharged in 24 hours to the out-patient department with a diagnosis of gastroenteritis, etiology unknown. She had been taking digitalis for several years.

Her present illness began with periumbilical pain, colicky, lasting one to two minutes and recurring every two to three minutes. Persistent vomiting began seven hours after onset of illness.

Physical examination revealed an obese 65-year-old female, appearing acutely ill. Temperature was 98.6° F., pulse 88, respirations 26. The abdomen was moderately distended and soft. No mass was felt.

Scout roentgenograms of the abdomen revealed small amounts of gas in the small intestine on the left side and no fluid levels. She was operated upon by Dr. G. J. Delany on the day of admission. The preoperative diagnosis was acute appendicitis. Inhalation anesthesia was discontinued in the induction stage when her systolic blood pressure fell from 150 to 60, and the operation was resumed one hour later under local anesthesia. About 800 cc. of clear straw-colored fluid was found in the peritoneal cavity. In the distal ileum the gut showed a yellowish fibrinous exudate for a distance of 1½ feet, and lying free in the lumen and almost completely obstructing it was a hard round mass about 4 cm. in diameter. A longitudinal incision was made in the ileum and a large gallstone removed and the incision closed.

She had an uneventful course and was discharged on the eleventh postoperative day to the Cardiac Clinic. She has remained essentially well.

Comment. It is probable that the symptoms which led to her one-day stay in the hospital in June, six weeks prior to operation, were due to the passing of the gallstone from the gallbladder into the intestine.

Case 10.—M. F. was a 75-year-old white female, admitted on August 1, 1948, with a chief complaint of persistent and progressive vomiting, constipation, and weight loss of one month's duration.

Her past history included occasional epigastric burning after meals and no severe postprandial pain or biliary colic.

Physical examination showed an essentially normal abdomen.

Gastro-intestinal roentgen ray examination revealed a large opaque mass at the pylorus, around which a small amount of barium passed into the intestine and into the biliary tree. The roentgen diagnosis was cholecystoduodenal fistula and a large gallstone obstructing the first portion of the duodenum.

Laboratory findings. Hg. 100 per cent; RBC 4.8 M; WBC 7300 with 57 per cent polymorphonuclears, 32 per cent lymphocytes, and 9 per cent monocytes. The blood Kahn was negative. The total serum proteins were 6.5 mg. per cent; albumen 3.8 and globulin 2.5; urea nitrogen 39; carbon dioxide combining power 67; prothrombin time 22. Electrocardiogram was normal.

On the sixteenth hospital day a laparotomy was performed by Dr. G. J. Delany. The pyloric antrum and first portion of duodenum were found to be densely adherent to

the liver in the gallbladder region. A hard mass, the size of a pullet egg, was felt in the first part of the duodenum. Because of adhesions the gallbladder could not be visualized. An attempt to locate the gallbladder by dissection, with the intent of dissociating the gallbladder and duodenum, failed. The pyloric antrum was opened longitudinally and the gallstone, seen in the duodenum, could not be delivered until the incision had been prolonged into the duodenum. The stone fragmented as it was being removed. The fistulous opening between the duodenum and gallbladder admitted the index finger. The incised wound in the stomach and duodenum was closed longitudinally.

She was discharged from the hospital on the eleventh postoperative day after an essentially uneventful course, has gained 20 pounds and feels well.

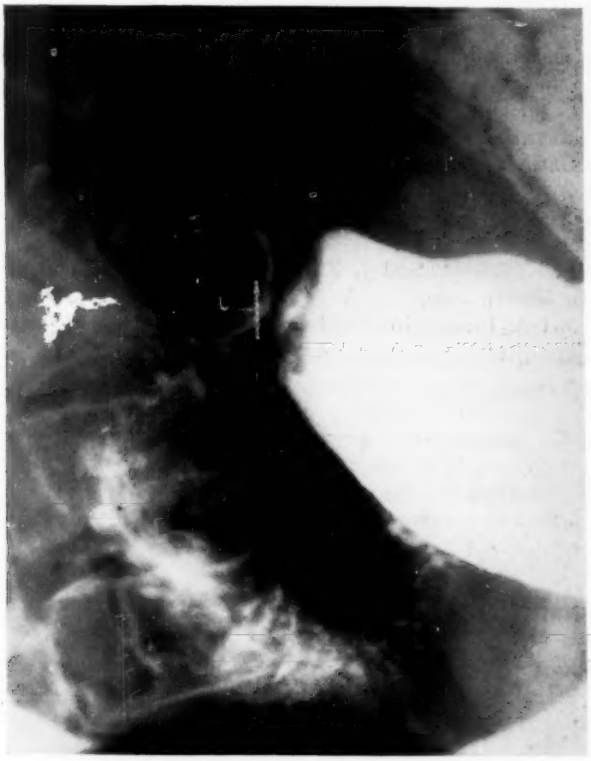

FIG. 4.—Film of gastro-intestinal roentgen ray series in Case 10 showing a gallstone in the duodenum and barium in the biliary tree.

SUMMARY

1. Ten cases of gallstone intestinal obstruction are presented, all with proved or presumptive cholecystoduodenal fistulas.

2. Urgent but not emergent operation is indicated, but only after adequate preoperative treatment, including hydration and restoration of electrolyte balance, gastro-intestinal intubation with suction, etc.

3. At the time of removing the intestinal gallstone, operation on the cholecystoduodenal fistula is contraindicated.

4. The importance of roentgen examination as an aid in differentiating gallstone from other types of acute small intestinal obstruction is stressed.

5. The high mortality of gallstone intestinal obstruction is an additional argument in favor of routine cholecystectomy for cholelithiasis unless contraindications forbid.

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METASTATIC MELANOMA OF THE BRAIN*

REPORT OF A CASE WITH UNUSUALLY LONG SURVIVAL PERIOD FOLLOWING SURGICAL REMOVAL

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METASTATIC MELANOMA of the brain is not a particularly rare intracranial tumor. In an extensive review of the literature on the subject, Courville and Schillinger[1] found that the incidence of involvement of the brain by growths of this character varied from nine to 68 per cent, as reported by different authors. In their own series they report an incidence of 50 per cent brain involvement in patients having metastases. The relative incidence of melanotic lesions in comparison with their own series of 107 cases of all varieties of metastatic brain tumors was 13 per cent. Quoting other authors, they found that this figure varied from two to 11 per cent. Moersch, Love and Kernohan[2] found 24 patients with brain involvement out of 347 cases of melanoma with local recurrence or metastases, an incidence of seven per cent. Twenty per cent of their cases with generalized metastases showed involvement of the central nervous system but this figure included a group without postmortem or operative confirmation.

The prognosis for a patient with a diagnosis of metastatic melanoma of the brain is, to say the least, extremely serious. In the series of Wortis and Wortis[3] the time from the onset of cerebral symptoms to death varied from seven days to four months. Six cases in the series of Moersch and his co-workers were operated on for intracranial lesions; four of these were in the left frontal lobe, one was cerebellar and one involved the third and fourth ventricles, pons and medulla. Of the four who survived the operation, two patients died one year after operation (Cases 5 and 16), another died six months after operation (Case 13), and no final information was obtainable on the fourth patient, although she was known to have become progressively worse following discharge from the hospital (Case 3). Of the 18 unoperated patients, 16 failed to survive more than seven months after the onset of neurologic symptoms, and the eventual outcome of the other two was not known. From a survey of their postmortem material these authors concluded that metastatic melanoma might occur throughout the organs of the body without involvement of the central nervous system and similarly, though to a lesser degree, the brain or the spinal cord might be the only site of involvement.

Courville states that the individual tumors are more apt to be unusually large when there are relatively few nodules in the brain. While the cerebral

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lesions are usually multiple, occasionally a solitary nodule is found at autopsy. It is only when a solitary lesion is suspected that Bailey[4] recommends any attempt to operate with the object of prolonging life. He states that the relief which is afforded by decompression lasts but a short time. Grant[5] is of the opinion that surgery, whether radical or palliative, is of no ultimate benefit to the patient in so far as prolongation of life is concerned. Moersch, Love and Kernohan[2] believe that complete removal of a solitary brain lesion is sufficiently helpful to be justifiable, and when extirpation is not possible they advocate palliative subtemporal decompression for the relief of symptoms of increased intracranial pressure.

That there may be a relatively benign type of intracranial melanoma was emphasized by Arnvig and Christensen[6] in 1939. They cited two cases from the literature which they believed represented this variety, and reported a case from Busch's Clinic in Copenhagen. The latter was a patient with a circumscribed melanoma of the fourth ventricle. The tumor was removed at operation, apparently completely, and the patient was living without symptoms one year later. Although the patient had numerous pigmented moles of the skin she showed no evidence of other lesions than the one in her brain, and the latter was believed to be primary.

Two other tumors, presumably similar to the one described by Arnvig and Christensen were reported in 1940 by Ray and Foot.[7] One of these was intraspinal and the other was between the cerebellar hemispheres at the cisterna magna. Both were circumscribed and were thought to have arisen from the meninges; in other words they were primary rather than metastatic melanomas. Microscopically the tumors were more like pigmented meningiomas, and the authors believe that they should be designated as such. The patients were alive and well one and one-half and four years after operation.

The following case is of interest in that the melanoma of the brain was apparently metastatic, yet the patient so far has had a useful survival period of nearly four years, following its removal.

REPORT OF A CASE

W. J. C. A 57-year-old insurance man was referred by Dr. Harry Roberts of Springfield, Massachusetts, and was admitted to the New England Deaconess Hospital on February 9, 1945, with the chief complaint of "attacks of dizziness."

Present illness. During the period of six months prior to admission, the patient had several unobserved attacks of unconsciousness. The seizures came without warning and lasted 4 to 5 minutes. The patient did not think that he had convulsive movements during the attacks and referred to them as "dizzy spells." One month before admission, he began having periods of nausea and vomiting, a roaring noise in both ears and about 3 transient spells of staggering gait. One week before admission, he fell down 4 steps during an attack of dizziness. He was unconscious for about an hour and was drowsy for a period afterward. His wife did not notice any paralysis following his unconsciousness but remarked that the patient could not say what he wanted to since this fall. He was hospitalized elsewhere at this time and roentgenograms did not show any evidence of fracture of the skull nor of metastases in the chest or pelvis. There had been no history of diplopia, scotoma or blurring of vision. In the year prior to admission he had some dull vertex headaches which were said to have been unusual.

Past history. On June 3, 1944, a left axillary adenectomy had been performed at another hospital for a painless swelling which had been present for six months. The tissue removed consisted of two glands, one measuring 4 cm. in diameter, the other 4.5 cm. in diameter, firm in consistency and, on being sectioned, presented a mottled dark brown to gray-brown color resembling melanin. Microscopically, the tissue represented a lymph node almost entirely replaced by tumor. The tumor cells were large, polygonal or elongated and fairly uniform in size. They were arranged loosely or occasionally in clusters, rests or along the stroma of vessels. The cytoplasm sometimes contained granular melanin pigment. The nuclei of the cells were usually large and oval, or sometimes lacunar shaped. Hyperchromic nuclei, multinucleate cells and mitoses were rare. The diagnosis was malignant melanoma (Fig. 1).

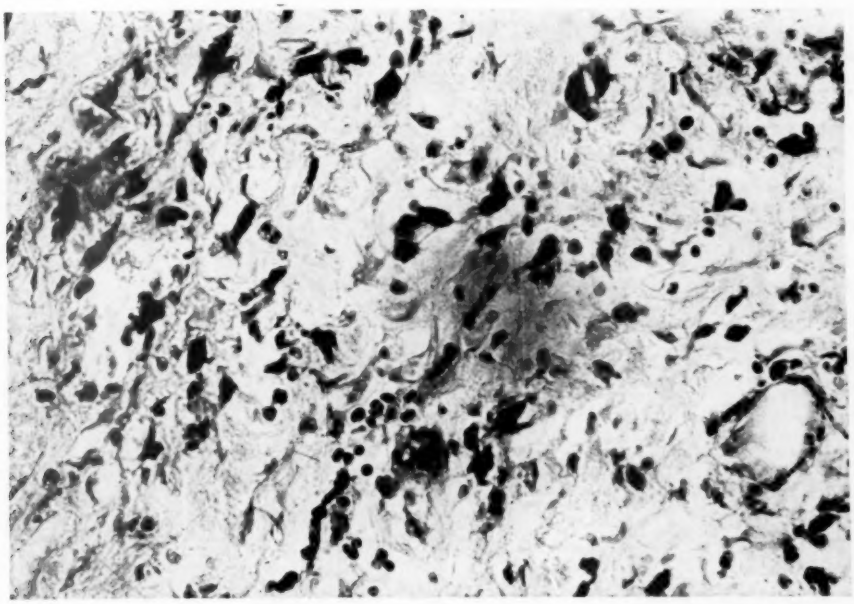

FIG. 1.—Photomicrograph from lymph node removed at Springfield Hospital (x 500) showing the shape and arrangement of the cells (Courtesy of the Pathologic Department of the Springfield Hospital).

On June 15, 1944, a left radical mastectomy was performed at the same hospital. Inquiry at that time into his previous history revealed that 14 months before the mastectomy the patient had had an irritated black mole of the left shoulder removed by a local surgeon who excised widely, knowing its potentialities. No microscopic sections of his mole have been available.

Physical examination. Routine clinical examination of the chest and of the abdomen was essentially negative. The integument was clear except for a well-healed left mastectomy scar without evidence of local recurrence. No glands were palpable in the groins, axillae or cervical regions.

Neurologic examination. The cranial nerves and visual examinations were normal although no funduscopic description was recorded.

Sensory examination disclosed a questionable loss of vibratory sensation over the right leg but otherwise the sensation was intact throughout in all modalities. Examination of the motor system showed a definite weakness of the right upper and lower extremities in all muscle groups, with some degree of clonus at the right wrist. The deep

reflexes were hyperactive throughout on the right side and there was a positive Hoffmann and Oppenheim sign on the right.

A roentgenogram of the chest showed the lungs to be clear except for a few small areas of density in the left first and second interspaces These did not suggest metastases and were probably the residue of a previous inflammatory process. The cardiac and diaphragmatic shadows were normal.

Ventriculography was carried out on February 12, 1945. The ventricular fluid was clear and under a slight degree of pressure. Both lateral ventricles and the third ventricle were well filled and were displaced to the right (Fig. 2). Depressing the anterior horn of the left ventricle was a rounded filling defect which suggested a tumor whose center was 2 cm. behind the meningeal channel (Fig. 3). The ventriculographic diagnosis was that of a tumor in the left frontoparietal area next to the longitudinal sinus.

The fact that the patient had developed an intracranial lesion after the removal of melanomas in the breast and axilla made it probable that we were dealing with a metastatic lesion, but this was not certain until an exploration had been carried out.

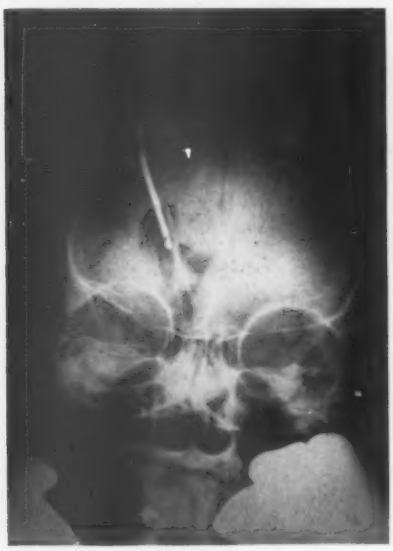

FIG. 2

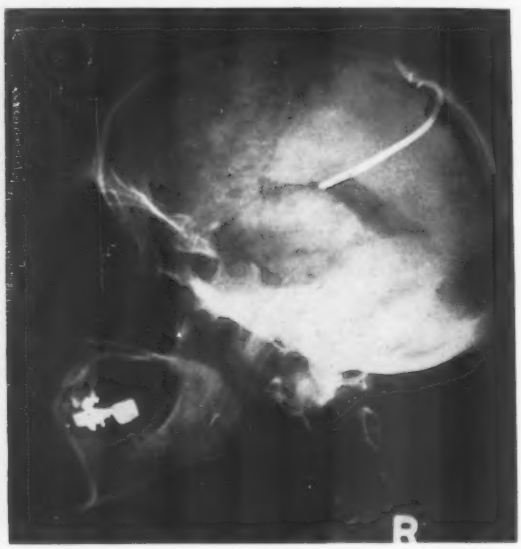

FIG. 3

FIG. 2.—Anteroposterior ventriculogram showing depression of the left ventricle and displacement of the ventricular system to the right.

FIG. 3.—Right lateral ventriculogram showing the curved depression made by the tumor in the anterior portion of the left ventricle.

Operation. A left frontoparietal bone flap was turned down on the same day that the ventriculogram was performed. A spherical, apparently encapsulated brownish-black tumor about the size of a duck's egg was removed without difficulty from the left frontal lobe. Its removal was accomplished by suction and coagulation around the mass and as it was easily encircled in its entirety, the excision was apparently complete. There was no evidence of any further tumor in the area exposed.

Postoperatively, the patient developed a slight aphasia and was drowsy for ten days. He improved gradually and when discharged on March 10, 1945, he was relatively asymptomatic.

PATHOLOGIC REPORT

Gross Description. The specimen consisted of a spherical mass of tissue measuring 4.5 cm. in diameter. The external surface was irregular, purplish-red and yellowish in

color, and moderately firm throughout. A cut section showed discrete nodules 1 to 1.5 cm. in diameter, moderately firm, some yellow with brown edges, others brown with black nodules up to 0.1 cm. in diameter.

Microscopic description. The tumor was composed of irregular sheets of oval and polygonal cells with large, round reticulated nuclei. Some cells were multinucleate but mitotic figures were infrequent. Many cells contained fine, granular cytoplasmic melanin. Usually there was no architectural pattern, but in some instances the cells lined up against the stroma of vessels. In places the tumor was necrotic. The tumor carried very little stroma (Fig. 4). The microscopic diagnosis was malignant melanoma.*

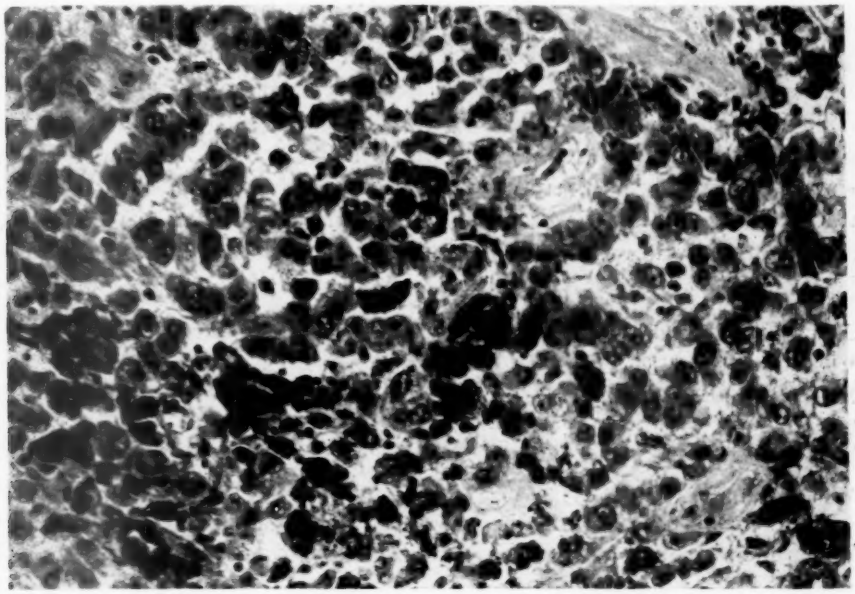

FIG. 4.—Photomicrograph of the tumor removed from the brain (x 400) to show the type of cell together with the contained melanin.

Subsequent reports. A letter from the patient dated December 31, 1946, (23 months after operation) stated that he was apparently well except for occasional convulsions.

On June 20, 1947 (2 years and 4 months after operation) he was seen and examined. He had had five major convulsions since operation but had otherwise been very well. His wife had also noted a transient spell without convulsion or unconsciousness characterized by aphasia in November, 1946. Subjectively, he had had no headaches, nausea or vomiting. He had shown no mental change and had been working 5 hours a day at his usual occupation. Examination at this time showed that his fundi were normal. There was slight deviation of the jaw and tongue to the left and the right upper extremity had a minimal weakness as compared to the left. The deep reflexes were hyperactive on both sides with an equivocal Babinski sign on the right. The remainder of the neurologic examination was negative. A general physical examination was likewise negative and the operative site on the left side of the chest showed no evidence of recurrence.

* We are greatly indebted to Drs. Meissner and Hicks of the Pathologic Department of the New England Deaconess Hospital for the gross and microscopic description of the tissues.

A letter from the patient's wife dated January 2, 1948 (2 years and 11 months after operation) stated that the patient continued to be very well and was at his usual office work every day. He was having occasional convulsive seizures about every five to six months, but these were not as violent nor as frequent as at first.

Last report. October 22, 1948, 3 years and 9 months postoperatively. At this time the patient's wife wrote that he was very well and at his usual occupation. He still had an occasional convulsive seizure but these were apparently becoming less frequent.

COMMENT

This case is unusual in that a surprisingly long and useful survival period has resulted from the removal of a metastatic melanoma of the brain. It is important since it illustrates the gratifying results that may be obtained occasionally following the extirpation of what appears clinically to be a solitary lesion. While the further prognosis must be extremely guarded the fact remains that the result has so far been highly satisfactory. One of the explanations as to how "aberrant" metastatic lesions can occur without evidence of involvement of the lungs was suggested by the anatomic studies of Batson on the vertebral vein system.[8]

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GIANT FIBRO-ADENOMA OF THE BREAST—"CYSTOSARCOMA PHYLLODES"*

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GIANT FIBRO-ADENOMA of the breast can be defined as a fibro-adenoma of large size that involves much of the breast. Not only must the tumor in the breast be a fibro-adenoma and large but it must also involve the major portion of the breast. A common name applied to this type of tumefaction is "cystosarcoma phyllodes." However, "cystosarcoma phyllodes" is a confusing term because the vast majority of such tumors are strictly benign while a few are malignant. The term "cystosarcoma phyllodes" as it has been used by most authors implies a huge tumor of the breast which is a benign fibro-adenoma in approximately 90 per cent of instances and a fibrosarcoma in the remainder. Such a term is therefore being used to connote a huge fibro-adenoma of the breast which, while usually benign, may be malignant. We shall confine our remarks to that group of tumors which are benign. It would seem appropriate to avoid the use of this term and to subdivide this group of cases according to whether the lesion is benign or malignant.

Many other descriptive terms have been applied to this tumor by various authors. Some of these are "cystic hydatid," "cellular hydatid," "cystosarcoma," "hydatid tumor of the breast," "serocystic tumor," "cystic sarcoma," "telangiectatic cystosarcoma," "proliferous cystosarcoma," "intracanalicular papillary fibromyxoma," "intracanalicular sarcoma," "intracanalicular myxofibroma," "sarcoma with lacunar cysts," "intracanalicular myxoma," "proliferating cystic tumor," "cystosarcoma mammae proliferum," "papilloma intracanaliculare," "intracanalicular fibroma," "intracystic mammary sarcoma," "cystofibrosarcoma," "pearly cystosarcoma phyllodes," "adenoma pseudosarcomatodes," "fibro-adenoma intracanaliculare papillare," "adenomyxofibroma intracanaliculare papillare," "fibrolipo-adenoma intracanaliculare sarcomatodes xanthomatodes mammae," "giant intracanalicular myxoma," "giant intracanalicular fibro-adenomyxoma," and "intracanalicular fibro-adenoma."

The literature on this tumor was summarized by Lee and Pack[6] in 1931. They were able to find reports of 105 cases up to that time and had four cases of their own. In the 91 cases in which the outcome was mentioned, there were six recurrences. One of these patients died from a pulmonary metastasis following a simple mastectomy. Three of 109 patients were men. The most

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salient clinical features were those of the presence of a precursory tumor, the rapid growth and the attainment of unusual size. Two of the 109 patients stated that lactation stimulated the rapid growth. One other patient was pregnant at the time the tumor was removed. The average age of 109 patients was 44.6 years. Twenty-one of the patients had ulcerated lesions of the skin, and in five others the tumor was adherent to the skin. In five patients, the growth fungated through the ulcer in the skin. The gross appearance of the tumor was characterized by the presence of polyps on the cut surface. Histologically, the appearance was that of fibro-adenoma with the stroma demonstrating myxomatous changes; this was a very constant feature in the group of cases reported by Lee and Pack. According to these authors, blood vessels are often thrombosed, and cholesterin crystals, foreign body giant cells and xanthomatous changes frequently occur in the tumor. Not all the polyps were covered by epithelium.

Owens and Adams[8] in 1941 reviewed the subject and were able to collect reports of 121 examples of this condition, 12 more than had been reported by Lee and Pack. They considered that the first case had been reported by Chelius in 1828 under the title "cystic hydatid of the breast." They reported one case of their own. They felt that the areas of myxomatous change in the stroma represented edema. They were of the opinion that the term "giant intracanalicular fibro-adenoma" would be a more proper term to express the true condition. Other cases which were not included in the article by Owens and Adams are those of Martin[7] in 1933, one case; Smith[10] in 1935, two cases; Touraine and Renault[11] in 1935, one case, bilateral; Crile[2] in 1938; one case, bilateral; White[12] in 1940, one case; Hopkins[4] in 1940, one case; Reed and Hiebert,[9] in 1942, one case, bilateral; and Cooper and Ackerman[1] in 1943, three cases. The lesion in the case reported by White recurred, eventually metastasized to the lung and, therefore, was malignant. The lesion in one of the cases reported by Cooper and Ackerman showed malignant changes, with invasion of the muscle and involvement of axillary lymph nodes. Although sarcomatous change apparently does occur in this tumor, Deaver, McFarland and Herman[3] stated, "Through what seems to have been some misapprehension of the true nature of the change, large tumors of the intracanalicular myxomatous type, in which tubules become distended into cysts and the intracanalicular formations become large enough to be easily seen by the naked eye, so that in a section of the fresh tumor they can be seen to project in the form of tea-like or finger-like eminences, have been described as cysto-sarcoma phyllodes. Such tumors are not sarcomas, and the name cysto-sarcoma phyllodes ought to be abandoned."

Many of the bilateral giant fibro-adenomas appear to have been in adolescent girls. However, bilateral enlargement of the breast not only is due to fibro-adenoma but also may be caused by simple hypertrophy. Of the four cases of massive bilateral enlargement of the breast reported by Keyser[5] in 1921, the lesions in two were the result of fibro-adenomatous proliferation and in two they were the result of simple hypertrophy.

PRESENT STUDY

Material. Records of 13 patients who had giant fibro-adenomas of the breast were found in the files of the clinic for the period from 1904 to 1943 inclusive. Two cases were excluded from this series because the fibro-adenoma showed malignant changes in the stromal cells. In order to be included in this series the fibro-adenoma had to involve the major portion of the breast (more than four fifths) and it had to be large (more than 500 Gm.).

TABLE I.—*Giant Fibro-adenomas of the Breast*

Patient's Age, Years	Lesions		
	Unilateral	Bilateral	Total
Less than 20	1	3	4
20–29	..	..	..
30–39	6	1	7
40–49	..	..	..
50–59	2	..	2
Total	9	4	13
Average age	37.3	19.7	31.9

Clinical data. Nine of the 13 patients showed involvement of only one breast while four showed involvement of both. Thus, the incidence of bilaterality in this group was approximately 30 per cent (Table I). In a group of 1074 cases of ordinary fibro-adenoma of the breast in which surgical removal was done at the clinic in the years 1935 to 1944 inclusive, the incidence of bilaterality was 6 per cent.

TABLE II.—*Bilateral Giant Fibro-adenomas of the Breast*

Case	Patient's Age in Years	Lesion			
		Greatest Diameter, cm.		Weight, Gm.*	
		Right Side	Left Side	Right Side	Left Side
1	13	20.0	15.0	2,290	1,600
2	13	13.5	13.5	760	780
3	15	15.0	16.0	1,660	2,110
4	38	19.0	17.0	2,500	2,530
Average	19.8	16.9	15.4	1,803	1,755

* Weight includes that of a small amount of adjacent breast tissue, fat and skin.

Bilateral giant fibro-adenomas of the breast. The pertinent data on the four cases in which the fibro-adenoma of the breast was bilateral are given in Table II. Both breasts attained, on the average, very similar sizes and weights, and two of the four patients were adolescent girls (Fig. 1). In one patient (Case 2) menstruation had not started. In the fourth case (Case 4) the enlargement of the breasts began during a pregnancy five years before bilateral

mastectomy was performed. In the other three cases, the enlargement had taken place within the year before mastectomy was performed. In this group, simple mastectomy was performed either in one stage or with a short interval (approximately a week) between the operative procedures on the two sides. Two of these cases (Cases 3 and 4) were previously reported by Keyser.

Unilateral giant fibro-adenoma. The pertinent data in regard to age, side involved, size and weight are given in Table III. Only one of these patients was an adolescent. On the other hand, one of the patients in this group (Case 13) was 11 years past the menopause. In six cases, the right breast was involved (Fig. 2), and in three, the left. A brief summary of the data in these cases follows:

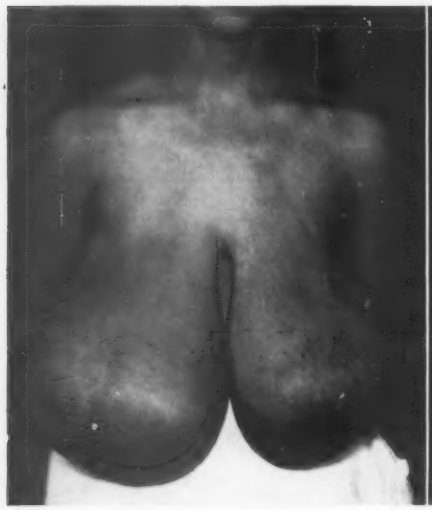


FIG. 1

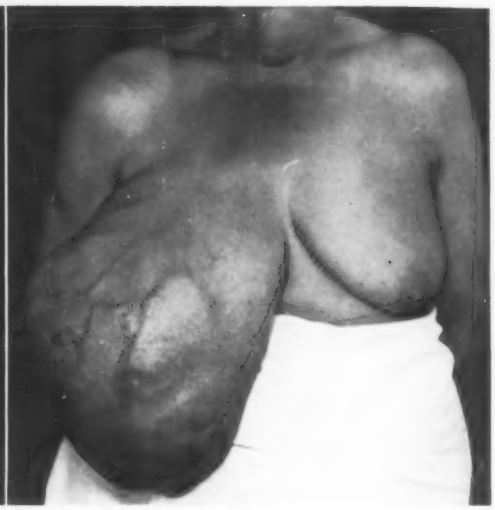


FIG. 2

FIG. 1.—(Case 1). Bilateral giant fibro-adenomas of the breast. The right is larger than the left.

FIG. 2.—(Case 13). Unilateral giant fibro-adenoma of the breast. Note the dilated veins over the tumor.

Case 5.—The right breast had been enlarged for seven years but rapid increase in size had occurred in the last two or three months. The patient had never menstruated. The left breast was also larger than normal. There was no ulceration of the skin. Simple mastectomy was performed on the right side for a giant fibro-adenoma, and this was followed by simple mastectomy of the left side six years later for chronic mastitis without fibro-adenoma.

Case 6.—For the past three years, gradual enlargement of the right breast had occurred, without relation to pregnancy. Simple mastectomy was performed.

Case 7.—For the past nine months, a gradual increase in the size of the left breast with retraction of the nipple had been noted. For two months, discoloration of the skin was present. The condition was not related to pregnancy. Simple mastectomy was done.

Case 8.—For nine years, a tumor in the right breast, which was first noted immediately after the birth of her first baby, had been present. It had been stationary in size

until the previous year and a half, during which it had doubled in size without relation to pregnancy. Simple mastectomy was carried out.

Case 9.—For the past year, gradual enlargement of the right breast had occurred without relation to pregnancy. There was no involvement of the skin. Simple mastectomy was performed.

Case 10.—Two years before operation, the left breast was five times the size of the right and very nodular. There was no history of the length of time required for the enlargement to occur. Simple mastectomy was done.

Case 11.—For two years, enlargement of the right breast had occurred following injury. The enlargement was not related to pregnancy. Simple mastectomy was performed.

Case 12.—For five months, there had been gradual swelling of the left breast, which was not related to pregnancy. Simple mastectomy was done.

Case 13.—For 25 years, a tumor in the right breast had undergone slow enlargement. It had doubled in size in the past 18 months. The patient had never been pregnant, and the menopause had occurred 11 years before. Simple mastectomy was performed.

TABLE III.—*Unilateral Giant Fibro-adenomas of the Breast*

Case	Side	Greatest Diameter, cm.	Weight, Gm.*
5	Right	20	2,125
6	Right	16	945
7	Left	17	1,850
8	Right	13	1,190
9	Right	15	1,940
10	Left	14	500
11	Right	20	2,950
12	Left	10	550
13	Right	28	5,400
Average		17	1,939

* Weight includes that of a small amount of adjacent breast tissue, fat and skin.

Pathologic aspects: *Gross characteristics.* Aside from the immense size, weight and diffuseness of giant fibro-adenomas, they differ in few details from other smaller fibro-adenomas. The diffuseness of such tumors in the breast was a noteworthy finding. In all instances, practically the entire breast was involved. At least three quarters of the breast was replaced by the fibro-adenoma, which presented itself as a lobulated, whitish mass whose cut surface had a mucoid appearance (Fig. 3). The fibro-adenomatous lobules were connected with one another. In no case could they be considered as multiple tumors. Finger-like projections, the result of intracanalicular extensions of fibrous tissue, could be seen frequently. Actual cyst formation was not a common manifestation in our group of cases.

Histopathologic features. The microscopic appearance was similar to that found in other fibro-adenomas except that myxomatous degeneration of the stromal cells was a fairly constant finding (Fig. 4). It appeared to us that at least some fibro-adenomas had started from multiple foci throughout the breast. This multicentric origin would also explain to some degree the large size. The stroma was, for the most part, inactive, the spindle cells being small and presenting no mitotic figures. In one case (Case 12), however, the stromal cells

were larger and looked more active than normal. In many of the cases, hyalinization of the stroma was taking place in areas (Fig. 5). The number of glands varied; in some cases there were few glands, in others, many. In practically every case there was a mixture of intracanalicular and pericanalicular types of fibrous growth. The epithelium lining the acini was most frequently a single layer of cells, although in a few cases the acini were lined by a double layer of cells. Necrosis of parts of the fibro-adenoma was a common finding. Adjacent breast tissue was demonstrable in all cases; this was frequently compressed and atrophic.

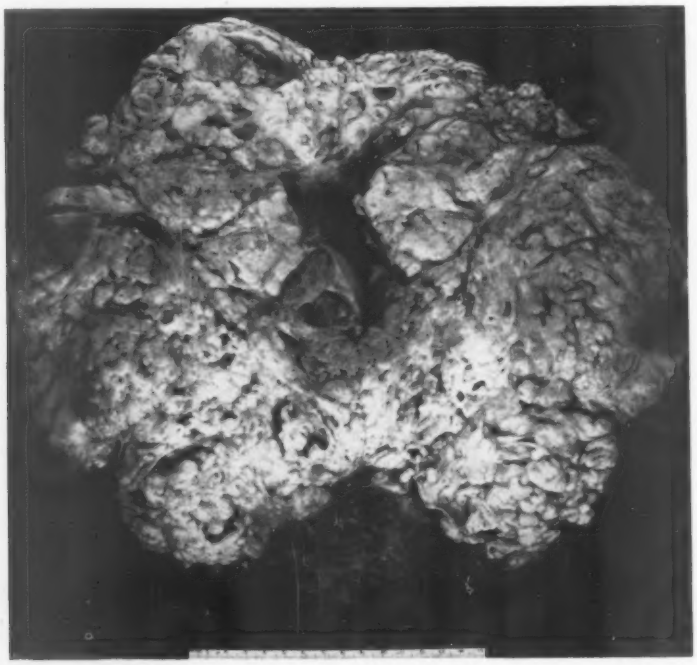
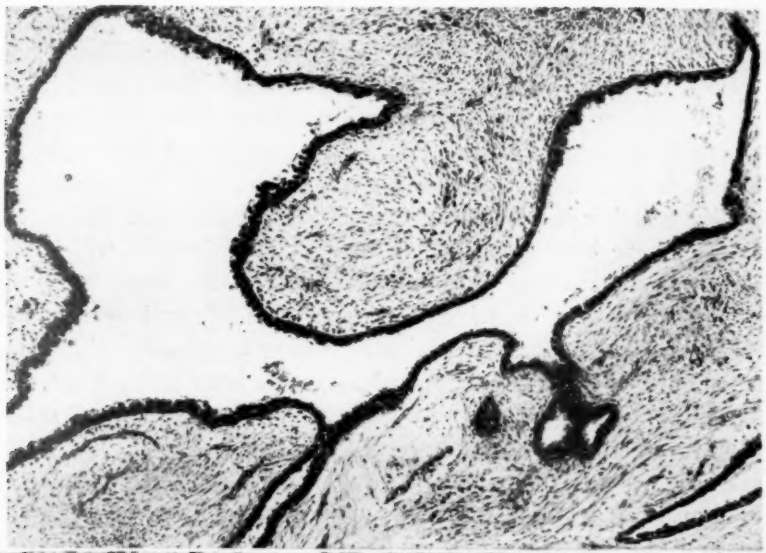


FIG. 3.—(Case 13). Cut surface of a giant fibro-adenoma of the breast. Note the leaflike structure and the cysts.

COMMENT

There appears to be some confusion in the literature regarding the incidence of malignancy of this neoplasm. There has been a small incidence of recurrence or metastasis or both, in the group of cases reported in the literature. In selecting the 13 cases which we are reporting, we have been careful to exclude all cases in which malignant change was evident. It would seem sensible, for purposes of clarity, to exclude all cases of malignant disease from the group of cases of giant fibro-adenoma of the breast. Furthermore, we are in agreement with Owens and Adams who expressed the opinion that the term "cystosarcoma phyllodes" should be avoided as it is not expressive of the true condition—the lesion is not usually sarcomatous. Certainly there should be a

FIG. 4



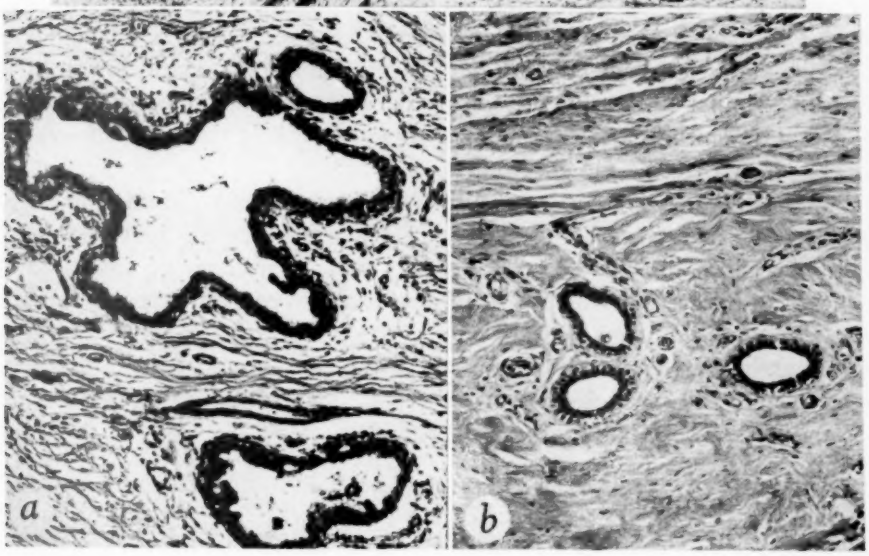


FIG. 5

FIG. 4.—(Case 9). Unilateral giant fibro-adenoma of the breast. Note the myxomatous change in the connective tissue (hematoxylin and eosin x50).

FIG. 5*a* and *b*.—(Case 1). Bilateral giant fibro-adenoma of the breast. Note the hyalinized stroma (hematoxylin and eosin x100).

sharp division between the benign and malignant counterparts of this neoplasm. Size alone is not evidence that a tumor is malignant.

Two important considerations which have a bearing on treatment should be discussed. The first is that giant fibro-adenomas of the breast are potentially malignant and should be so considered until proved otherwise. Approximately 10 per cent have proved to be malignant. When malignant, it is the stroma which changes, and the resulting neoplasm is a fibrosarcoma. The other consideration is that they involve practically the entire breast. Surgical treatment should be a simple mastectomy and not excision of the tumor. A thorough histologic examination of many parts of the neoplasm should be done to determine whether it is benign or malignant.

Our cases have been divisible into two groups: those in which the fibro-adenoma was bilateral and those in which the involvement was unilateral. Two of the four patients in which the tumor was bilateral were adolescents; in the fourth patient the tumor originated during pregnancy. Both breasts in all four patients enlarged simultaneously. As has been pointed out, this incidence of bilaterality is considerably higher than for a series of consecutive cases of ordinary fibro-adenoma.

One of the problems is to determine whether a diffuse fibro-adenoma has or has not arisen from a pre-existing tumor in the breast. In only two cases (Cases 8 and 13) was there a history of a lump in the breast before the breast started to assume immense proportions.

The age incidence in our series of cases of unilateral giant fibro-adenoma was very similar to that in cases of ordinary fibro-adenoma. This would suggest that a giant fibro-adenoma involving one breast is similar to an ordinary fibro-adenoma except for size.

The pathologic appearance of a diffuse fibro-adenoma differs only slightly from that of an ordinary fibro-adenoma. The difference can be accounted for mainly by size. The ulceration of the skin and the necrosis of the tumor can be explained on a vascular basis and does not indicate benignancy or malignancy of the underlying tumor. No one can adequately explain what causes myxomatous changes in the stromal cells of giant fibro-adenomas. Myxomatous degeneration is much commoner in giant fibro-adenomas than in ordinary ones although it does occur in the latter.

SUMMARY

We have reported 13 cases of giant fibro-adenoma of the breast; in nine the lesion was unilateral, and in four bilateral. No cases in which malignant change was demonstrated have been included in this report. Simple mastectomy is the treatment of choice because of the involvement of much of the breast and the malignant potentialities.

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LIGATION OF THE INFERIOR VENA CAVA DURING PREGNANCY*

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DESPITE THE INCREASINGLY large body of literature on the subject which has accumulated during the past decade, there is still no uniformity of opinion concerning the management of phlebothrombosis. Medical and surgical approaches to the problem each have eminent champions. As experience widens, each method would seem to have definite advantages and disadvantages, indications and contraindications.

In all probability, any final and universally accepted outline of treatment for managing this emergency will be based upon individualization of the particular case. During the present period of study and of the correlation of data from various sources it would seem especially important, then, to focus attention upon cases in which phlebothrombosis is accompanied by other complications, for what may be proper treatment in one case may very likely prove to be highly improper in another.

Recently we performed ligation of the inferior vena cava in a case of phlebothrombosis which complicated early pregnancy, and subsequently we searched the literature to find case reports similar to our own. But, while vena cava ligation in postabortal and puerperal states has been reported rather frequently,[1, 2] we have been unable to find another report of this operation having been performed in early pregnancy. One case, to the best of our knowledge, has been reported in which the operation was performed in the last trimester. In 1929 Del Pino and Masciotra[3] described vena cava ligation in a patient seven months pregnant who had suffered an injury during the course of a kidney operation. Labor ensued the day after ligation and the patient was delivered of a premature infant who did not survive. The mother recovered uneventfully.

More recently, Foulkes[4] reported the case of a patient in whom thrombosis of the inferior vena cava developed following pelvic cellulitis. The obstruction was complete and permanent and yet the patient delivered a living, term infant ten years later following a relatively uneventful pregnancy. Her chief complaint during pregnancy was hemorrhoids, which were accompanied during the last trimester by anal prolapse, and which finally became so severe that labor was induced at 36 weeks. The first stage of labor was complicated by uterine inertia and lasted 36 hours. She was delivered spontaneously of a living infant after a second stage of ten minutes. The placenta

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was delivered spontaneously five minutes later and the patient's postpartum course was entirely uneventful.

Collins[5] has observed three patients upon whom vena cava ligation had previously been performed who became pregnant and carried their babies to term without ill effects.

While ligation of the inferior vena cava should not be undertaken lightly, it is gradually gaining wide acceptance as a proper and safe method of preventing embolism in certain instances following phlebothrombosis. The present case, in which the patient continued to term without difficulty, demonstrates the feasibility of the operation in early pregnancy. Certainly, it would seem that the life-saving nature of the procedure more than offsets any danger to the maintenance of the pregnancy itself. Situations requiring the operation will seldom be encountered in pregnancy but, once the indications for it are clear, in our opinion vena cava ligation should be carried out without delay.

CASE REPORT

A 21-year-old primigravidous graduate nurse underwent appendectomy for acute appendicitis on April 19, 1947, at approximately 8 weeks uterogestation. Her last normal menstrual period had begun on February 7, 1947, making her estimated date of confinement November 14. Inspection of her uterus at the time of laparotomy confirmed the presence of an intra-uterine pregnancy.

Following the operation she was given *Cyclogesterin* daily. She began leg and breathing exercises immediately upon reaction from her anesthetic, walked within 36 hours of the operation and was out of bed walking daily thereafter. Our usual policy of having postoperative patients walk considerably earlier than this was modified because of her pregnancy. Her only postoperative temperature elevation was a single reading of 99.4 degrees F. on the first postoperative day. Thereafter, her temperature was 98.6 degrees F. or less. Pulse and respiratory rate were normal. Routine examinations of the patient's lower extremities, made twice a day throughout her hospital stay, did not reveal evidence of thromboembolic disease. She had no varicose veins. Past history regarding peripheral vascular disease, thromboembolic disease or injury to the extremities was negative. Her postoperative course in the hospital was entirely uneventful, the midline abdominal wound healed by first intention and she was discharged, still pregnant, on her seventh postoperative day.

Five days after her discharge from the hospital, during which interval she had been up and about at home, she experienced a sudden, agonizing pain throughout her entire left lower extremity. The leg immediately turned blue and cold. The patient recognized the critical nature of her distress, obtained an ambulance and was readmitted directly to the operating room 30 minutes after the onset of her pain. She reported that for 24 hours before the occurrence of her acute pain she had experienced vague, fleeting cramps in her left thigh and calf, which were so mild that she had attached no importance to them.

Upon admission, the entire left lower extremity was deeply cyanotic and very cold. The dorsalis pedis, posterior tibial, popliteal and femoral pulses could not be found. The leg was not swollen, nor was there local tenderness in the calf or thigh. The right leg appeared to be entirely normal. General physical examination, including examination of the heart, was negative, except that the patient was obviously in great pain.

Under the impression that she was suffering from an acute occlusion of the left iliac artery, the patient was prepared for surgery and was operated upon 20 minutes after her admission to the hospital. A low left rectus transperitoneal incision was made, the

posterior peritoneum being opened over the common iliac artery. Both this vessel and its branches were found to be pulsating normally and there was no evidence of arterial embolus. However, the left common and external iliac veins contained a poorly organized thrombus 15 cm. in length, the tail of which extended to the inferior vena cava. The vena cava was accordingly doubly ligated below the renal veins after extraction of the clot. The right iliac veins were not examined because of the manipulation of the pregnant uterus which would have been required. The second, third and fourth lumbar sympathetic ganglia were blocked with 1 per cent procaine and the wound was closed. At the conclusion of the operation, the left leg was warm, dry and of good color.

Twenty-four hours after operation leg measurements showed the left calf and thigh to be 1.5 cm. greater in circumference than the right, the largest difference that was noticed during the patient's subsequent course.

On her fourth postoperative day she complained of moderate pain and tenderness in the left calf and thigh. This was the first and only discomfort she noticed following ligation. One per cent procaine block of the first, second, third and fourth sympathetic ganglia was performed with complete relief. She was allowed out of bed wearing elastic stockings and bandages on her ninth postoperative day. The highest temperature during her convalescence was 99.2 degrees F. Throughout her hospital stay she was given mild sedatives and *Cyclogesterin,* and at no time did she threaten to abort. At the time of her discharge from the hospital circumferences of the left lower extremity were approximately 1 cm. greater than those of the right. Venous pressures were not obtained.

The patient's subsequent course was entirely uneventful. Increase in the circumferences of the left leg over the right varied from 0.5 cm. to 1.5 cm. Six weeks after ligation she confessed that she had been taking long walks in the country with her husband. Since neither appreciable edema nor discomfort followed these walks, limitation of activity was left to the patient's discretion. Noticeable varicosities of the abdominal wall did not develop, as were reported in Foulkes' case, though infra-red photography was not employed in an attempt to demonstrate them. Small hemorrhoids did develop during the last trimester. They were not severe and disappeared following parturition.

She entered into spontaneous labor during her thirty-ninth week of gestation and was delivered, following episiotomy, of a 6-pound, 2-ounce living female infant by outlet forceps following an uneventful 8-hour labor. The placenta was removed manually 15 minutes after delivery of the infant because of partial separation. Estimated total blood loss was 125 cc., and the uterus remained well contracted.

The patient's puerperium was uneventful except for transitory pain in the left calf on her first postoperative day. Examination of the leg was negative and the pain was permanently relieved by 10 grains of aspirin. Uterine involution progressed at a normal rate. Leg measurements were equal. She was discharged in good condition on her tenth postpartum day, having been up and about since her first postpartum day.

Two months later, she was again working as a general duty floor nurse. She had no complaints and repeated physical examinations were entirely normal. She wore her elastic stockings at work but admitted, 6 months after delivery, that she frequently neglected to wear them when she was off duty, without any apparent ill effects. At her last examination, 6 months postpartum and 12 months after ligation of the vena cava, her extremities appeared to be entirely normal.

DISCUSSION

Etiologic factors concerned with intravascular clotting have long attracted the attention of physiologists and surgeons and are too well known to warrant a complete review here. The possible contributory importance of pregnancy itself is, however, worthy of mention.

Bland and Goldstein,[6] using Bogg's modification of the Brodie-Russell technic, concluded after a study of 400 gravid women that there is an appreciable tendency of blood to clot more quickly in pregnancy than in the non-gravid state. They found that whereas only 36 per cent of 100 normal, non-pregnant women had a clotting time which ranged between 1.5 and 2.5 minutes, clotting was completed in 97.2 per cent of their gravid subjects in less than 2.5 minutes. A number of other investigators have been unable to find any appreciable difference between the coagulability of blood in pregnant and non-pregnant individuals, however.

If blood does clot more readily during pregnancy, it is apparently the result of the increased fibrinogen which is present during gestation. Dieckmann,[7] together with a number of others, has demonstrated this increase repeatedly, even though it is occasionally only a slight one. It is, apparently, the only alteration of blood in pregnancy which is significant as regards the process of coagulation. Blood platelets, prothrombin time and blood calcium remain within normal limits.

Recently, Cummine and Lyons,[8] in a study of intravascular thrombosis, reviewed a previous report of Lyons[9] which indicated that the transformation of fibrinogen to fibrin occurs in two stages and that an intermediate substance, fibrinogen B, is a precursor of fibrin. They feel that delayed postoperative thrombosis (in their classification that which occurs more than 24 hours after operation) is indirectly caused by the presence of fibrinogen B associated with venous stasis. These factors, they believe, cause platelet disintegration and intravenous thrombin is formed. Stasis again plays a part in preventing the normal metabolism of the fibrin which is formed. They conclude that factors which contribute to the development of delayed postoperative thrombosis appear to be pyogenic infection and/or tissue necrosis, which result in the formation of fibrinogen B in the circulating blood. This results in increased platelet fragility which, coupled with venous stasis, gives rise to intravenous thromboplastin. Aided by low coagulation time, intravenous thrombin is then formed. Thrombosis then develops as the result of the fibrin which is formed, aided by venous stasis.

Whether or not increased amounts of fibrinogen B in circulating blood may result from the existence of a pregnancy itself is not known. One of us (R. L. Y.) plans to report the results of such a study in the near future. Should increased amounts of fibrinogen B be shown to occur, intravascular clotting in pregnancy could be easily explained, for the tendency to venous stasis in pregnancy is well known and the alleged easy coagulability of blood in pregnancy has already been commented upon.

In the case we are reporting, the correct diagnosis—phlebothrombosis of the left common and external iliac veins—was not made until the time of operation. Except after severe and extensive trauma, acute arterial thrombosis rarely occurs in the presence of a normal heart. Despite lack of evidence of pathologic changes in the heart, a preoperative diagnosis of arterial

occlusion was made because of the unusually intense reflex arterial spasm in the affected extremity, which obliterated arterial pulsations and resulted in a cold, clammy and deeply cyanotic extremity.

Reflex arterial spasm of mild degree probably accompanies many cases of venous thromboembolic disease, but it is rather uncommon to find it so great. This syndrome, known as pseudoembolic phlebitis, phlegmasia caerulae dolens, and to some authors as the "blue phlebitis of Gregoire,"[10] has been described in the American literature on a number of occasions, but has still not received the attention it deserves. Ochsner and De Bakey,[11] who have studied this phenomenon extensively, call attention to the fact that in some instances spasm has been so great that actual gangrene has occurred. They have demonstrated the cause of the spasm to be vasomotor impulses originating in the involved segment of a localized thrombophlebitic process and transmitted to the artery over the sympathetic nervous system.

Actually, we feel that the diagnostic error was chiefly one of academic importance, since we firmly believe that ligation of the inferior vena cava below the renal veins is the treatment of choice for phlebothrombosis of the iliac and/or femoral veins, regardless of whether or not pulmonary embolism has occurred. A number of authors share this belief, and for several reasons. The likelihood of an embolus arising from the "uninvolved" leg in cases of apparent unilateral disease is well known.[12, 13] Greenstein[14] observed that venous thrombosis of the lower extremities was bilateral in every instance in which postmortem examination was made. Obviously, nothing short either of bilateral femoral or iliac ligation or of vena cava ligation will protect the patient from such a silent thrombus. Moses[13] has outlined the disadvantages of ligation at levels lower than the vena cava. Chief among these are the dangers of extension of the process following femoral ligation owing to the difficulty, and occasionally the impossibility, of estimating the extent of the process clinically before operation. In a correlation of clinical and operative findings, Moses reports that tense edema extending above the knee does not occur from a simple phlebothrombosis confined below the inguinal ligament and that when this type of edema does occur, the clot is too closely adherent to the wall of the femoral vein to permit effective and safe thrombectomy. He feels that in such instances, ligation of the vena cava should be carried out as a primary procedure. Further, postoperative edema has been shown to be less following ligation of the vena cava than following ligation of the femoral or iliac veins.[15, 16]

A lower left rectus incision, such as was made in the case we are reporting, is definitely *not* the one of choice through which to ligate the vena cava, but, as we have demonstrated, it can be done when necessary. Had we recognized the true nature of the disease process in our patient, we would have elected the extraperitoneal approach to the vena cava, a simple and highly satisfactory method which, incidentally, can be accomplished in less time and with less skill than are required for bilateral ligation of the iliac veins.

The transperitoneal route is preferred by some, however, and if there is doubt as to the diagnosis, it is probably the wiser method.

As we have already mentioned, arguments over the comparative merits of vein ligation as opposed to the use of anticoagulant drugs in the treatment of phlebothrombosis continue. During the past few years our own attitudes have gradually changed from favoring anticoagulants to favoring surgical intervention. Despite a large body of literature to the contrary, we have not always found the control of anticoagulant therapy a simple matter. Individuals vary greatly in their response to these drugs, especially to Dicumarol. On several occasions we have seen prothrombin times in large adults drop to dangerous levels following the administration of only 50 or 100 mg. of the drug.

Especially in patients who are pregnant, the use of anticoagulant drugs alone would seem hazardous. Spontaneous abortion or the spontaneous onset of labor are apt to occur during the course of any acute disease. Should this happen, the control of hemorrhage might prove trying, although the maternal complications encountered in five parturient women to whom heparin was administered by Barnes and Ervin[17] were limited to two hematomas in episiotomy wounds. Excessive maternal bleeding was not noticed, although more than one-third of the babies born to these mothers, and to another group of 14 mothers to whom Dicumarol had been given, showed prolongation of the clotting time and in some cases prolongation of both bleeding and clotting times. Moreover, Von Sydow[18] has recently reported a case of severe hypoprothrombinemia in an infant born of a woman who had been taking Dicumarol, and cautions against the use of this drug in pregnancy except under extraordinary circumstances.

Collins[19] and others have called attention to the importance of the use either of lumbar sympathetic nerve interruption at the time of vena cava ligation or of routine postoperative sympathetic blocks to minimize complications from the ligation and to overcome reflex spasm. We are sure that an important factor in our patient's recovery from the operation was the use of this latter procedure. Either sympathectomy or sympathetic block should, in our opinion, always accompany vena cava ligation.

Extraction of the clot distal to the site of ligation is not universally recommended. It is probable, however, that more satisfactory collateral circulation can be achieved, and at a higher level, if this is done. This higher level of collateral circulation, incidentally, is probably the reason that less edema is reported after vena cava ligation than after femoral and iliac ligation. O'Neil,[15] in a study of collateral pathways for venous return following interruption of the inferior vena cava, has found it to be more than adequate for efficient circulation. Even in pregnancy, where demands upon pelvic circulation are greatly increased, our own case and those we have reviewed in which pregnancy followed ligation or thrombosis of the vena cava demonstrate that fears concerning the possible lack of competency of the collateral circulation are groundless.

SUMMARY

1. A case of early pregnancy is reported in which the inferior vena cava was ligated because of phlebothrombosis which developed after appendectomy. A review of the literature fails to reveal reports of similar cases.

2. The etiology of postoperative thrombosis is reviewed, especially in its relation to pregnancy. Suggestions concerning the possible etiologic effects of pregnancy itself are made.

3. The advantages of the surgical approach to the management of phlebothrombosis are outlined and ligation of the inferior vena cava is recommended as a safe and effective procedure where phlebothrombosis complicates pregnancy.

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CONGENITAL ANEURYSM OF SUPERIOR VENA CAVA*

REPORT OF ONE CASE WITH OPERATIVE CORRECTION

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PRIMARY ANEURYSMS of venous structures are a considerable rarity. The discovery of a large, probably congenital aneurysm of the superior vena cava, with apparent operative correction is felt to be sufficiently unusual to justify a case report. The author has not been able to find a report of a similar case either in life, or upon autopsy examination.

The patient, Mr. H. S., a 19-year-old white male college student, was seen in consultation on February 17, 1948. The only reason for consultation was the discovery of a large mass in the region of the superior mediastinum, on the right. The family history was not unusual. There was no history of antecedent serious illness, and no history of previous injury to the thoracic cage. He was born at full term without any difficulties associated with the labor, and his mother had experienced no unusual diseases during the period of pregnancy. The patient had never been known to show evidence of cyanosis; hemoptysis was denied, and there were no unusual sensations in the thorax, and there had been no dyspnea. He had been able to take part in strenuous physical exercise without difficulty. He had no knowledge of any thoracic abnormality until a 70 mm. screening roentgen ray film was taken in January, 1948. An unusual superior mediastinal shadow was noted, and therefore the patient was recalled and a complete roentgen ray study carried out.

It was of interest to discover that this patient had a similar 70 mm. roentgen ray film taken November 22, 1946, and this showed the lesion to be present at that time, but apparently smaller in size. No previous roentgen ray examination of the patient had been performed.

The findings on the roentgen ray studies are presented in Figures 1 and 2. Figure 1 shows the inspiration chest roentgen ray taken November 22, 1946, while Figure 2 shows the P. A. view roentgenogram taken on full expiration. The patient was subjected to a very intensive roentgen ray investigation. Fluoroscopy and film studies were carried out February 18, 1948, by Dr. T. F. Leigh. His notes, made at that time, read as follows: "Fluoroscopy and films of the chest demonstrated a unilateral enlargement of the superior mediastinum on its right side. This mass appeared to lie anteriorly, was sharply outlined laterally, but could not be seen on its medial border. The mass markedly changed shape when visualized in deep inspiration and deep expiration. A further change of shape from the standing to the horizontal position was noted. It was of homogeneous density and contained no calcium. There was no displacement of the trachea or the esophagus by the described mass. It appeared to move paradoxically in relation to the aortic pulsations. It could not be determined whether its movements were due to intrinsic or transmitted pulsations. The lungs otherwise appeared normal. The heart was normal in size."

On February 26, 1948, angiocardiographic studies were carried out by Doctor Leigh (See Figs. 3 and 4). The description of his findings at that time read as follows: "Films of the heart and great vessels were made in the right posterior oblique position after the injection of 70 per cent Diodrast into the right antecubital vein. The contrast media appears to show a fusiform dilatation of the superior vena cava. A part of this dilatation probably also includes the right innominate vein. The vena cava has a trans-

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FIG 1

FIG. 2

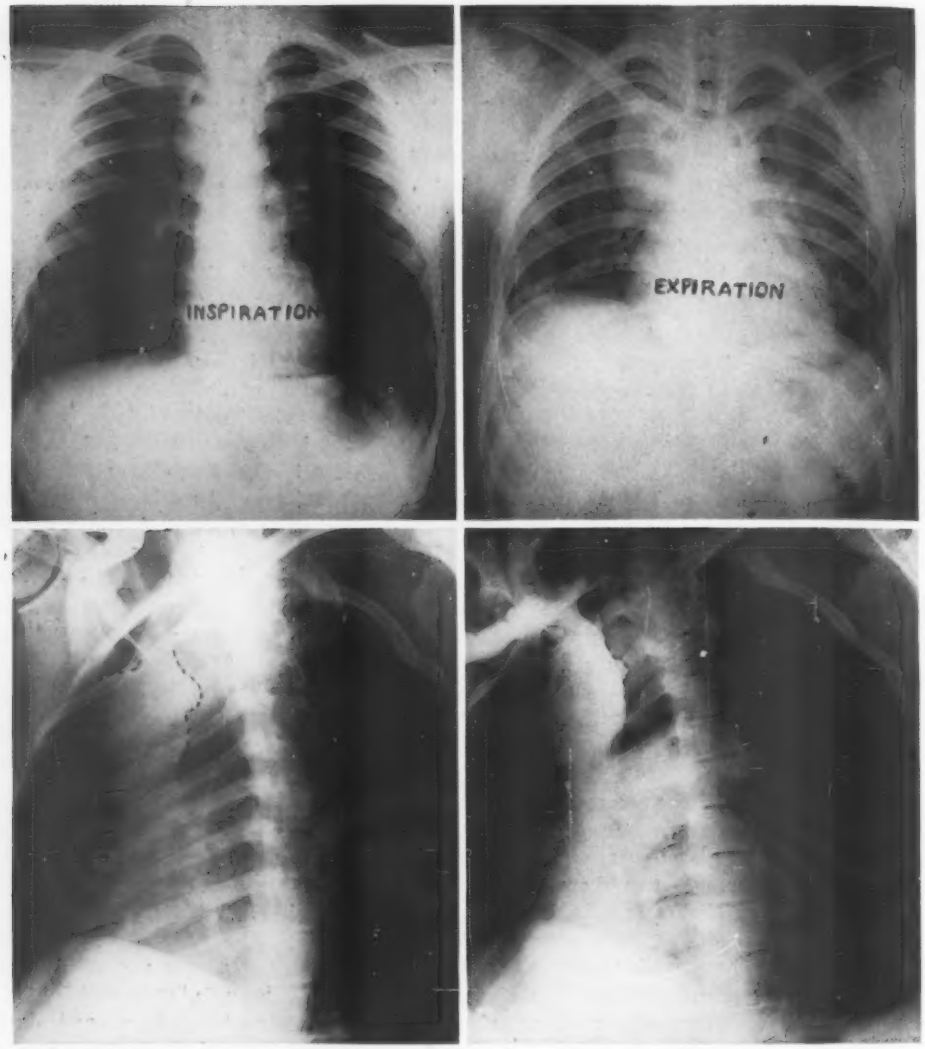


FIG. 3

FIG. 4

FIG. 1.—Postero-anterior roentgen ray projection February, 1948. Note the right paramediastinal shadow demonstrates considerable translucency.

FIG. 2.—Postero-anterior roentgen ray projection February, 1948. Compare this film taken on full expiration with the inspiration film shown in Figure 1.

FIGS. 3 and 4.—Figure 3 demonstrates the findings noted on the primary positioning film taken in the right oblique. This position was found to give maximal visualization of the lesion. Figure 4 denotes the filling of the aneurysmal area in the right innominate vein and superior vena cava. Note irregularity on postero-medial surface, which is too far posterior to be a part of the left innominate vein.

verse diameter of 5 cm. It contracts down to apparent normal size just before entry into the heart. The borders of the mass can be seen extending approximately 1 cm. beyond the border of the opaque column in some areas. This would indicate that the vena cava has either a thick wall or that there is a compression of the vena cava causing its dilatation through broadening and flattening by an extra-vascular mass. There is no apparent obstruction to the passage of the opaque media. The examination discloses no other abnormal findings in relation to the cardiac chambers, pulmonary vascular bed, or first portion of the aorta."

On physical examination the patient appeared to be a very healthy individual. There were no definable abnormal physical findings. The blood pressure in the right arm was 110/80, in the left arm was 120/80, and in the right leg was 132/85. The venous pressure readings were determined in both arms: Right arm 130 mm. blood, left arm 109 mm.

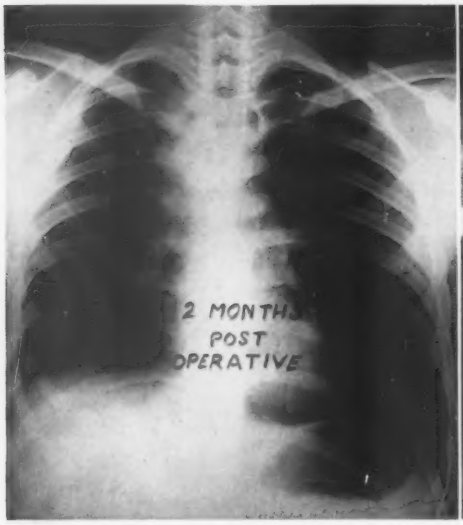
The patient was studied by the method of cardiac catheterization, but these studies appeared somewhat to confuse the issue. The pressure readings within the superior vena cava, right auricle and right ventricle were within normal limits. There appeared to be a one volume per 100 increase in the oxygen content of the blood obtained from the superior vena caval area in contrast to those obtained from the right auricle and right ventricle. With the catheter in the superior vena cava, Diodrast was injected and failed to show the dilatation noted on the previous angiocardiographic studies. These studies seemed to indicate that the superior vena cava itself was not enlarged, but distorted by a nearby mediastinal tumor. The variance in the oxygen content of the blood in the superior vena cava in contrast to that within the cardiac chambers suggested the possibility of an arterio-venous communication.

In view of the unknown nature of the mass plus evidence of enlargement of the mass in the roentgen ray studies over a two-year period, it was felt advisable to recommend exploratory thoracotomy. On July 23, 1948, exploratory thoracotomy was carried out under endo-tracheal gas-oxygen-ether anesthesia. The antero-lateral approach was used with subperiosteal resection of the anterior two-thirds of the right third rib. On entering the pleural cavity some dense adhesions were noted between the posterior and medial surfaces of the right upper lobe, and the adjoining chest wall and mediastinum. Palpation revealed an irregular ovoid firm mass in the superior mediastinum with nodular enlargements on the medial and posterior surface. The upper lobe was dissected free from the mediastinum, and a large mass in the region of the superior vena cava and right innominate veins was seen. The two nodular areas described appeared to be daughter aneurysms.

Multiple grape-sized, small aneurysms were found to be present on the antero-medial surface of the large aneurysmal area in the superior vena cava, and this aneurysmal enlargement was also found to involve the proximal 2 cm of the major azygus vein as it entered into the superior vena cava. The right phrenic nerve was found to be firmly adherent to the aneurysm, and was carefully dissected away. The aneurysmal wall appeared to be very thin except in the region of the two daughter aneurysms which apparently contained clots. The one on the posterior surface had the appearance of a false sac. The entire superior vena cava and right and left innominate veins were carefully dissected free and surrounded by a double sheet of polythene cellophane which had been prepared by boiling. The cellophane was sutured in place by means of a No. 4-0 deknotel silk to nearby structures, and the aneurysm completely surrounded, including the proximal 4 cm. of the right innominate vein, and the proximal 3 cm. of the azygus major vein. The point of entry of the left innominate vein into the aneurysm was protected by non-reactive cellophane. A long free graft of pleura was then obtained from the posterior chest wall and used to surround the phrenic nerve throughout the area in which it would lie over the region of the aneurysm surrounded by polythene cellophane. The chest wall was closed in layers in the usual manner. The patient

withstood the procedure well. The postoperative course was remarkably smooth, and he was discharged on the sixteenth postoperative day. There was no visible evidence of increased venous pressure in the upper extremities at the time of discharge and the venous pressure readings at that time were almost exactly the same as those prior to operation.

The patient's physical activities were moderately restricted for the first three months following operation, and he was not allowed to indulge in strenuous exercise until six months after surgery. He was studied frequently by means of fluoroscopy and roentgen ray examination. During the postoperative period there seemed to be some slight increase in the size of the mass during the first two months following operation (See Fig. 5). On January 21, 1949, six months after the operative procedure, the patient was again subjected to angiocardiographic studies (See Fig. 6). Doctor Leigh's



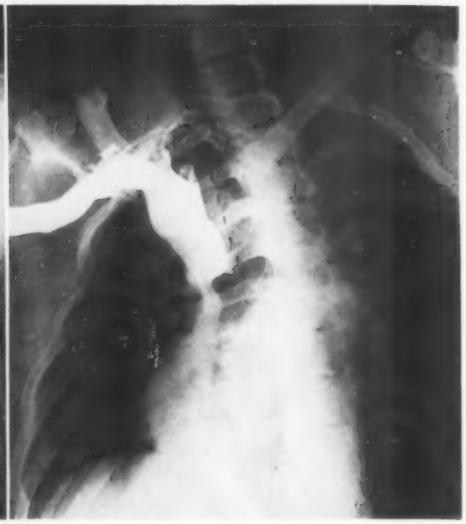


FIG. 5 FIG. 6

FIG. 5.—Postero-anterior roentgen ray projection taken September, 1948. Note evidence of moderate enlargement of the paramediastinal shadow which is expected during the first three months after Polythene cellophane application.

FIG. 6.—Angiocardiographic study performed January, 1949. This shows definite decrease in the size of the lumen of the aneurysmal area and definite thickening of the aneurysmal wall.

report reads as follows: "Repeat angiocardiographic studies of the right innominate vein and superior vena cava reveal a moderate reduction in the size of the aneurysm in these vessels. Just distal to the aneurysm there is a mild narrowing of the vena cava, but this does not appear to be obstructing the flow of the contrast media into the heart. Opinion: Reduction in size of aneurysm postoperatively of the right innominate and superior vena cava veins. Moderate constriction of the superior vena cava just distal to the aneurysm."

Patient has had repeated studies of venous pressure during the intervening months, and there has been no alteration in these findings. Examination of venous pressure on February 3, 1949, revealed the venous pressure in the right arm to be 128 mm. of blood, and that in the left arm to be 122 mm. of blood. There has been no evidence of abnormal collateral venous circulation appearing over the thorax or upper extremities. Patient has been totally asymptomatic, and has been able to continue a full schedule in the University.

SUMMARY AND CONCLUSIONS

The roentgen ray and clinical findings of a patient having a congenital aneurysm of the superior vena cava and right innominate veins has been described. The diagnostic measures utilized, the roentgen ray findings, and the findings at the time of operation have been described in detail because of the apparent unique character of this lesion. It is noted that the aneurysm of the superior vena cava showed changes in size and shape with inspiration and expiration comparable to other thin-walled cysts of the mediastinum. The angiocardiographic studies performed by means of injection of 70 per cent Diodrast into the antecubital vein proved to be of considerably more value than did the study carried out with a ureteral catheter within the lumen of the aneurysmal structure. The cardiac catheter studies were not thought to be of value in this patient, but actually appeared to confuse the issue. It is also believed, after direct visualization of the extremely thin wall of the lesion at the operating table, that the catheter could constitute an extremely dangerous procedure, and in fact, might even have been responsible for the false saccular aneurysm on the posterior surface of the lesion. It is felt that the character of the wall of the aneurysm would not have allowed any attempt at plication methods, and that the only satisfactory method of attack was by means of the use of polythene cellophane. It is also considered to be extremely important that this material not be prepared by soaking in alcohol. The alcohol may dissolve the di-acetyl phosphate contained in the substance which is necessary for the production of the marked fibroblastic reaction. The patient has been observed over a period of seven months following the operative procedure, and it is not felt that further obliteration of the lumen of the vena cava should occur due to the surrounding polythene cellophane. Comparison of pre- and post-operative angiocardiographic visualization of the aneurysmal structure has shown a very definite improvement in the size of the lesion, with marked thickening of the aneurysmal wall.

PRIMARY SPLENIC HEMATOCYTOPENIA

A CASE REPORT*

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DURING THE PAST TEN YEARS progress has been made in the study and treatment of a group of cases which present the objective findings of a large non-tender spleen with a concomitant destruction of peripheral blood cellular elements. In this comparatively small group of reported cases the clinical history, hematologic and pathologic studies and physical examinations have been similar but not identical to the findings necessary to justify conclusively the diagnosis of any one of the more common described forms of hypersplenism, *e.g.*, Idiopathic Thrombocytopenic Purpura; Splenic Anemia (Banti's Syndrome, Congestive Splenomegaly); and Hemolytic Icterus (Spherocytic Anemia).

CASE REPORT

History. A white nurse, 32 years old, was admitted to the Mary McClellan Hospital on September 21, 1948, because of a mass in the left side of the abdomen. She gave no history of having been exposed to medicinal or chemical agents. The family history was irrelevant, and she gave no history of a recent infection or abdominal trauma. In July, 1948, she first noted a mass in the left upper abdominal quadrant. During the following two months the mass grew rapidly in size until it produced a sense of epigastric fullness which was aggravated by the ingestion of food. Except for moderate weakness she presented no other subjective complaints.

Physical Examination. The physical examination was non-contributory except for a large, smooth, non-tender mass occupying most of the left side of the abdomen. The mass extended from beneath the left costal margin above, downward into the pelvis and across the midline to the right side. A notch was palpated just beneath and slightly to the right side of the umbilicus.

Laboratory Findings. The significant findings were related to the blood studies. On September 21, 1948, the hemoglobin was 8.7 Gm. per 100 cc.; erythrocytes, 2,890,000; leukocytes, 700; polymorphonuclears, 28 per cent; lymphocytes, 72 per cent; eosinophils, 1 per cent; stab cells, 2 per cent. The peripheral blood smears were not remarkable, and revealed no significant increase in reticulocytes. A sternal puncture was done and the bone marrow studies revealed a marked erythroblastosis. The white blood cell elements were of normal distribution. Erythroblasts, 62; myeloblasts, 1; promyelocytes, 3; myelocytes, 1; metamyelocytes, 5; polymorphonuclears, 12; lymphocytes, 15. The platelet count was 41,280 cells per c.mm.; hematocrit, 29 per cent; coagulation time, 5.5 minutes; bleeding time, 2.75 minutes and clot retraction, 24 hours. The sedimentation rate was normal, and the prothrombin time, (Quick's method), 17 seconds (40 per cent concentration). The icterus index was 2; cephalin flocculation test, 1 plus; Van den Bergh-negative-direct; the erythrocyte fragility test-hemolysis began at 0.45 per cent saline and was completed at 0.36 per cent. The red cell diameter was within normal limits.

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Progress. The patient received iron and liver therapy for a period of two months, at the end of which time the hemoglobin was 12 Gm. per 100 cc. and the erythrocyte count 3,750,000. A splenectomy was performed on November 24, 1948. A few cubic centimeters of clear, straw colored fluid were present in the peritoneal cavity. The liver was not appreciably enlarged. Its surfaces were smooth, the edges were sharp and its color was normal. During the procedure the patient received 2,500 cc. of whole blood. During the first three postoperative days the patient was given nasal oxygen. Her convalescence was essentially uneventful and she was discharged from the hospital on December 10, 1948. She was last seen on March 24, 1949, at which time she was asymptomatic and presented no objective findings. She has been doing general hospital duty as a nurse since six weeks after being discharged from the hospital. On February 24, 1949, the erythrocyte count was 4,310,000; white blood count, 7,950; platelets, 238,000 per c.mm.

Pathology. Gross: The spleen measured 27 by 15 by 4 cm. and weighed 1.93 Kg. after 2 liters of blood had drained from the viscus. The capsule was thin, tense and light

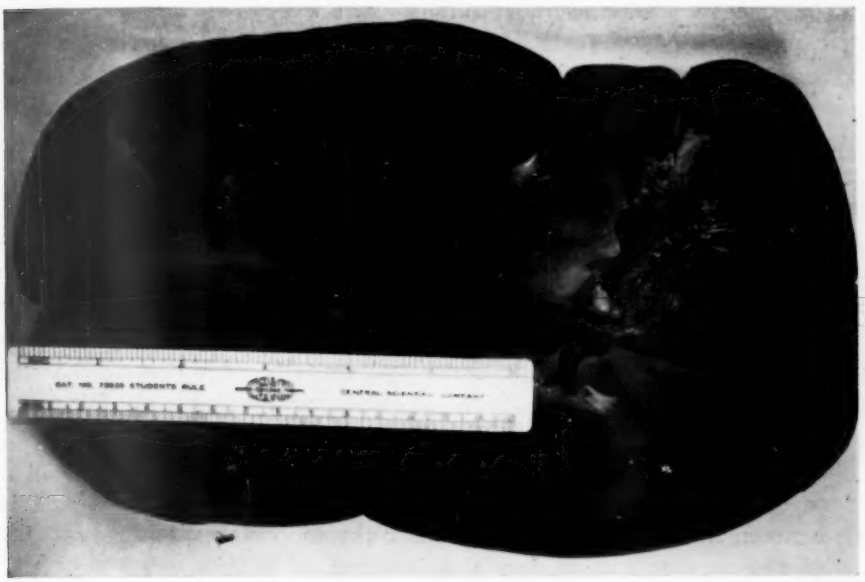

FIG. 1—Spleen weighing 1.93 kilograms.

slaty-gray-red in appearance. The cut surface was soft in consistency, moist and dark red in appearance. The splenic pulp was almost semi-liquid, oozing large amounts of dark red blood.

Microscopic. The capsule was moderately thickened and fibrosed. The trabeculae were few, inconspicuous, dispersed and small. The Malpighian corpuscles were small, quiescent, widely scattered and sparse; no germinal centers could be identified. The red pulp was engorged with blood and the sinusoids dilated. The cells lining the sinusoids contained large amounts of coarse, brownish black pigment, but a large proportion of these pigment granules were scattered through the red pulp.

Stains with Prussian blue showed that a fairly large amount of the intracellular pigment gave a deep blue reaction indicating the presence of iron. The free pigment did not give the iron reaction.

DISCUSSION

In 1942 Wiseman and Doan[1] first described a syndrome which they called primary splenic neutropenia. Their criteria for making the diagnosis of this syndrome were: an enlarged non-tender spleen, a severe neutropenia with variable anemia and thrombocytopenia, and a bone marrow revealing panhyperplasia without maturation arrest. They advocated splenectomy for the treatment of this syndrome, and reported several cases. Their first case was successfully operated upon by Dr. George M. Curtis, Colombus, Ohio, in October, 1939. During the past nine years several case reports have appeared in the literature, *e.g.*, Wiseman and Doan,[1] Moore and Bierbaum,[2] Jobin and Larochelle,[3] Salzer, Ransohoff and Blatt,[4] Langston, White and Ashley,[5] Kinsey and Bingham,[6] McClean and Coleman,[7] and Palumbo.[8]

In 1946 Doan and Wright[9] introduced a new descriptive term, primary splenic panhematopenia, to designate a syndrome characterized by a nonselective depression or elimination of all peripheral blood cellular elements despite a compensatory panmyeloid hyperplasia. When a review of cases of primary splenic neutropenia has been made it is conceivable that many of the cases might have been classified according to this new nomenclature. Kracke[10] uses the term primary splenic panhematocytopenia to designate the group of syndromes which result from hypersplenism producing a depression of two or more of the peripheral blood cellular elements. When all blood cellular elements have been depressed he emphasizes the great importance of differentiating the syndrome from hypoplastic anemia. Lahey[11] has stressed the importance of demonstrating the functional capacity of the bone marrow, and has re-emphasized the essentiality of excluding agnogenic myeloid metaplasia before a splenectomy is performed.

As the result of a marked thrombocytopenia, purpura may be present in primary splenic panhematocytopenia, and a differential diagnosis must be made between this syndrome and idiopathic thrombocytopenic purpura. The blood picture may and often does simulate that of Banti's syndrome. Like primary splenic neutropenia it may possibly be a subgroup of Banti's syndrome; however, it presents no objective findings of portal hypertension or liver damage. Studies of the spleen reveal no histo-pathologic features described for Banti's syndrome. A careful history, bone marrow studies, blood determinations and physical examinations will aid in differentiating this syndrome from other diseases in which there is a splenomegaly, *e.g.*, Kalazar, Hodgkin's disease, Felty's syndrome, leukemia, Gaucher's disease and other lypodystrophies.

The technical procedure of removing such a large spleen as the one herewith presented demands an adequate exposure of the splenic pedicle. We found it convenient to ligate the splenic vessels as they coursed above the tail of the pancreas. The vessels were exposed without difficulty through the gastrocolic omentum. This method of approach was described by Dr. A. O. Singleton.[12] We believe that postoperative intestinal distention, a common

development after splenectomy, was prevented by employing nasal oxygen intermittently during the first three postoperative days.[13]

The cause of this syndrome is not known, and opinions differ in predicating its etiology. Doan and Wright[1, 9] suggest that the spleen destroys the various cellular elements by a process of phagocytosis carried out by the macrophages in the spleen. Haam and Awny[14] postulate the existence of a humoral factor which is capable of either destroying the cellular elements or making them destructible.

SUMMARY

A case of primary splenic panhematocytopenia with recovery has been presented and the diagnosis discussed. The close relationship of this condition to other forms of hypersplenism has been reiterated and the importance of excluding the presence of agnogenic myeloid metaplasia prior to splenectomy has been re-emphasized. After all studies have been carefully analyzed and a presumptive diagnosis of the syndrome made, a splenectomy is indicated.

(Appreciation is expressed to Drs. C. E. Forkner, C. A. Finch and L. K. Diamond of Boston for their consultations. Thanks are extended to Dr. J. Lebowich of Saratoga Springs for his aid in interpreting the blood and pathologic studies.)

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EPIDERMOID CYST OF THE SPLEEN*

REPORT OF A CASE

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CYSTS OF THE SPLEEN, distinct from their rarity, are of two-fold interest. They usually present an intriguing and difficult diagnostic problem, and when removed provide an interesting source for speculation as to the probable mode of origin. It is not within the scope of this paper to give a general discussion of splenic cysts, but rather to present another case of epidermoid cyst of the spleen with the results of a survey of the literature for additional proved cases. The most recent review was made by Shawan[43] in 1933 so this review is continued from that date.

Before describing the case it is, perhaps, worthwhile to review splenic cysts. One is impressed with the great number of types that have been reported by various authors. Most cysts can be readily grouped using Fowler's[16] system. Although his major divisions into true and false cysts are understood and used frequently, some confusion exists as to the sub-groupings so the following outline of Fowler's classification is presented:

A. Primary or True Cyst:
   1. Congenital
      a. Infoliation cyst
      b. Dilatation or ectatic cyst
   2. Traumatic
      a. Infoliation cyst
      b. Dilatation or ectatic cyst
   3. Inflammatory
      a. Infoliation cyst
      b. Dilatation or ectatic cyst
   4. Neoplastic
      a. Dermoid
      b. Epidermoid
      c. Lymphangioma
      d. Cavernous angioma
   5. Parasitic
      a. Ecchinococcus

B. Secondary or False Cyst: (possessing no true epithelial lining)
   1. Trauma
   2. Inflammation
      a. Tuberculosis, perisplenitis, etc.

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3. Degeneration
   a. Infarction secondary to thrombosis, embolus, endarteritis, ruptured aneurysm, etc.

PRESENTATION OF A CASE

J. G. (SMH No. 277376), a 17-year-old, white schoolgirl was admitted to Strong Memorial Hospital on March 16, 1948.

The patient stated that she was in good health until 2 weeks before admission, when she awoke in the morning with a feeling of general malaise. That night she began to have pain centering about the umbilicus which at times was quite sharp and radiated to the left flank. That day she noted 3 loose bowel movements. The pain continued steadily for the next 4 days and increased in severity. On the fifth day she was admitted to another

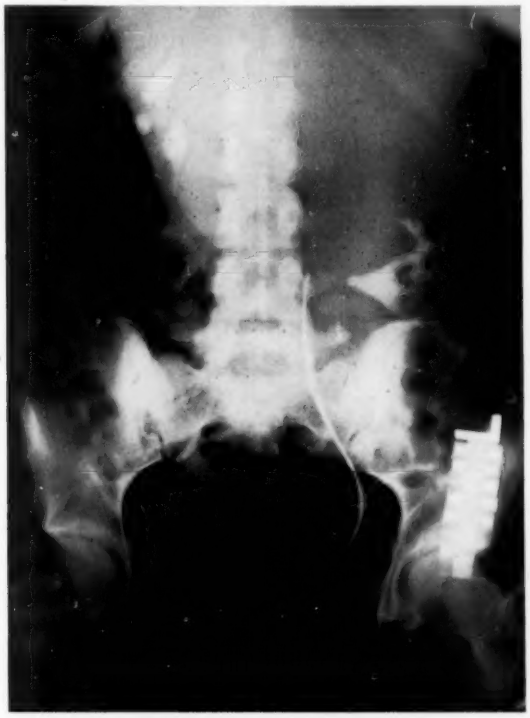

FIG. 1.—Retrograde pyelogram showing the left kidney pushed down to pelvic brim by the cyst.

hospital where roentgenograms of her stomach and kidneys were made. She had no urinary complaints and denied any feeling of pressure or undue prominence of her abdomen.

Her past health had been good, and the family history revealed nothing remarkable.

She was a well-developed, white, young female who appeared somewhat pale, but who was alert and cooperative.

Abnormal physical findings were limited to the abdomen where a globular mass 15 cm. in diameter was visible in the left upper quadrant extending below the umbilicus and to the right of the midline. Its surface was smooth and slightly tender. The mass moved with respiration but no true descent could be ascertained. It could not be balloted bimanually. No spasm or tenderness was noted elsewhere.

Examination of the blood showed a hemoglobin of 14.2 Gm., a red blood count of 3.3 million and a white blood count of 10,600. Differential white blood count was polymorphs, 70 per cent; lymphocytes, 24 per cent; monocytes, 3 per cent; eosinophils, 2 per cent; and basophils, 1 per cent. Urinalysis revealed no abnormal findings. Chemical determinations of numerous blood constituents were made, all of which were within normal limits.

Roentgenographic examination revealed no intrinsic lesion of the upper gastro-intestinal tract. On fluoroscopy of the chest the left diaphragm was elevated and its movement was somewhat limited as compared to the right diaphragm. The medial portion of the dome of the left diaphragm was pushed far to the right and encroached on the right lung base. The esophagus and cardiac portion of the stomach were pushed far to the right with

FIG. 2

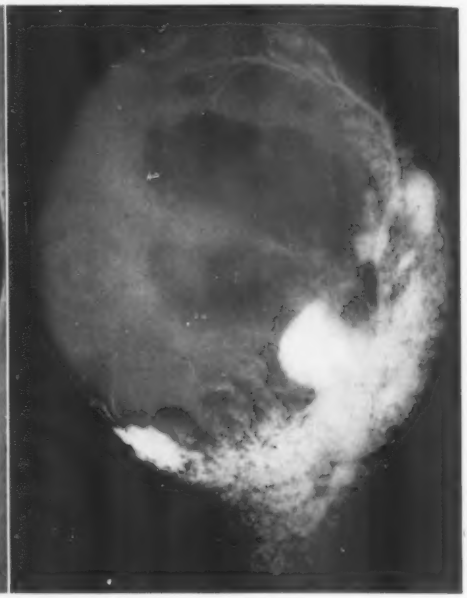

FIG. 3

FIG. 2.—Anterior view of cyst and remaining splenic tissue at the inferior pole.
FIG. 3.—Roentgenogram of specimen following injection of splenic artery and vein with radiopaque dye.

considerable compression of the latter. The pyloric portion of the stomach and the entire duodenum were also displaced to the right of the midline. On the films the jejunum and ileum were seen to be pushed downward and to the right, and the splenic flexure was displaced downward. Retrograde pyelograms showed that the left kidney had been pushed down to the pelvic brim, with no blunting or alteration of the major calyces (Fig. 1).

Laparotomy was performed on March 18, 1948, under sodium pentothal and gas-oxygen-ether anesthesia, through a transverse incision in the left upper quadrant. A large, reddish mass, which had the appearance of spleen, presented in the wound. It was attached widely to the diaphragm and had pushed the stomach over to the right side of the abdominal cavity. The portion of the tumor under the costal margin seemed to be cystic, so a needle was inserted and 3350 cc. of chocolate colored fluid containing glistening particles of cholesterol were withdrawn. The mass became flabby and easier to handle. Accordingly, the spleen was freed and removed. A transfusion of 500 cc. of whole blood was given during the procedure. The operation was well borne.

The patient was discharged on the twelfth postoperative day after an uneventful convalescence.

The specimen, which weighed 1100 Gm., was a large, collapsed cyst measuring 19 by 19 by 10 cm., intimately attached to firm, red, normal appearing splenic tissue at the inferior and infero-lateral margins (Fig. 2). The spleen proper measured 6 by 4 by 3 cm. and fanned out to encircle the cyst wall for a short distance along the medial border. On the lateral border it extended for a greater distance and almost reached the superior aspect of the cyst. The great vessels of the spleen lay on this rim of firm splenic tissue. The splenic tissue represented about one-fourth of the volume of the specimen and the cut surface appeared normal.

The remaining tissue was an intrasplenic cyst constituting three-fourths of the volume of the specimen. The firm, rubbery capsule of the spleen was studded with many greyish-white and greyish-brown firm plaques of various sizes, the largest measuring 6 by 8 cm. The larger ones rose above the surface and felt almost cartilaginous. The plaques were present over the entire cyst, but were more numerous over the superior, antero-superior and inferior aspects. Small, dense, fibrous adhesions were seen on the antero-superior aspect where the mass had been in contact with the left lobe of the liver.

The cyst was filled with Pick's solution. The vessels were then injected with a radiopaque, colored latex solution outlining the vessels over the wall and within the splenic tissue. Red dye was injected into the arterial tree and blue dye into the venous. No dye was visible grossly within the large or small cystic spaces (Fig. 3).

After bisecting the specimen, the wall of the cyst was found to be almost paper-thin and translucent in some areas while in others the fibrotic plaques reached a thickness of 0.7 cm. On the infero-medial aspect some small cysts lined by greyish-white tissue and measuring 1 to 1.5 cm. in diameter lay within the rim of splenic tissue (Fig. 4). The lining of the large cyst consisted chiefly of grey, fibrous appearing tissue, but in the inferior aspects adjacent to the splenic tissue the lining presented areas of dark tissue resembling splenic tissue over which many fibrotic bands stood out in honeycomb fashion, forming niches and dark recesses resembling the chordae tendinae of the heart.

FIG. 4.—Cut section showing splenic tissue at the inferior pole and coarse, fibrous trabeculations on the intraluminal aspect of the cyst.

Histologic sections from the normal appearing splenic tissue revealed a thin, fibrous connective tissue capsule from which trabeculae projected down into a pulp. The dilated splenic sinuses were engorged with erythrocytes. Many splenic follicles composed of densely packed, small, round cells were scattered throughout. Many large cystic spaces were seen which were single or multi-loculated. They possessed an endothelial or no lining, and contained either red dye granules, blue dye granules, or were empty (Fig. 5).

Sections through the wall of the large cyst adjacent to the splenic tissue revealed a thick zone of dense, laminated, fibrous connective tissue which in some areas was almost completely hyalinized. Much of the intraluminal aspect of the large cyst was lined by flattened, elongated, spindle-shaped cells which here and there thickened into a stratified, pavement-type of epithelium simulating epidermis. Intracellular bridges were seen near the basal layer. However, the pavement epithelium was unusual in that the cells on the inner aspect were large and more polyhedral while those close to the basement membrane

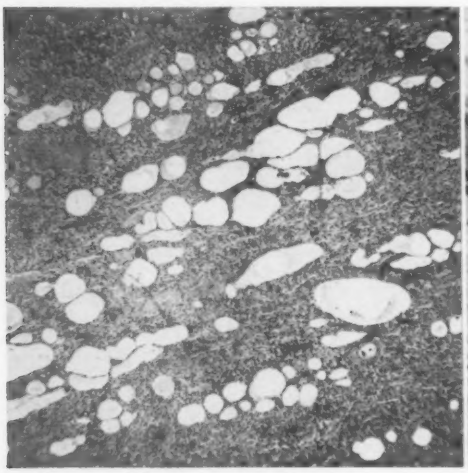

FIG. 5

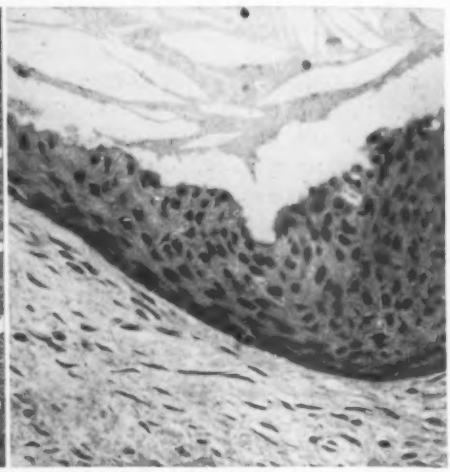

FIG. 6

FIG. 5.—Low power view of grossly normal splenic tissue showing multiple, small cystic spaces.

FIG. 6.—High power view of stratified pavement epithelium lining the wall of the cyst. The acicular spaces in the lumen represent previous site of cholesterol crystals.

were more flattened. No signs of keratinization were noted (Fig. 6). In the zone between the thick, fibrous wall and the largest remnants of splenic tissue, but not sharply demarcated from it, were a number of small, cystic spaces. Some of these contained dye granules and were indistinguishable from those described in the splenic pulp. Others possessing a partial lining of stratified pavement cells contained only granular, basophilic material and acicular spaces representing cholesterol deposits.

Sections from the thick, cartilage-like portions of the cyst wall which was not surrounded by splenic tissue revealed it to be composed of thick, dense, relatively acellular, hyalinized, connective tissue with only a few islands of epithelial lining. Within the wall, compact clusters of small, circular, endothelial-lined spaces containing erythrocytes were present which simulated compressed splenic pulps. At one edge of this tissue were many large macrophages containing hemosiderin granules.

Diagnosis. Splenic cyst, epidermoid type.

REVIEW OF THE LITERATURE

The following cases of epidermoid cyst of the spleen have been reported since the survey of Shawan[43] in 1933:

Harding, H. E. (1933).[22] A 22-year-old female had noted abdominal swelling for seven years. She complained of gradual increase in size with production of a nagging sensation and occasional nausea. The mass lay to the left of the umbilicus and projected downwards. A splenic cyst containing homogenous, mucoid material lay entirely within the splenic capsule. The lining consisted of stratified squamous epithelium with distinct intracellular bridges.

Montgomery, et al. (1938).[34] A seven-year-old girl was found to have a mass in the left upper abdomen. A splenic cyst, 12 by 8 by 3.8 cm. was removed which contained 520 cc. of chocolate colored fluid. The cyst wall was lined partly by stratified squamous epithelium.

Gosset, et al. (1939).[21] A 16-year-old girl sustained a severe fall injuring her left side. Pain persisted in the left hypochondrium for one month. She became aware of a swelling in that area nine months later. A poorly outlined mass in the left hypochondrium "the size of a child's head" was found which moved slightly with respiration. The cyst measured 22 by 18 by 14 cm. Stratified squamous epithelium lined the deep recesses of the cyst.

Lereboullet, et al. (1939).[28] An eight-year-old boy had a mass in the left hypochondrium. It was fixed at the costal margin and was not ballotable on bimanual palpation. A cystic spleen, weighing 850 Gm. was removed. On section a unilocular cyst 8 cm. in diameter was noted containing 300 cc. of clear, yellow fluid. A distinct line of cleavage between the cyst and spleen was present. Only laminated fibrous tissue was seen lining the cyst in most areas. Some of its diverticula were lined with stratified squamous epithelium.

Paul (1943).[38] A 19-year-old girl noted a lump in the left upper abdomen which had become painful. The mass extended from below the left costal margin to the umbilicus. A splenic cyst was removed containing thin, brown fluid and cholesterol crystals. The specimen contained one large cyst without a lining and many small cysts in the wall lined by stratified squamous epithelium.

Parker and Brown (1948).[37] A 16-year-old Negro female had a large painless mass in the left upper quadrant. The specimen removed from the abdomen was a cystic spleen in which was found a cavity measuring 13 by 10 by 11 cm. and an adjacent, smaller multilocular cyst measuring 4 cm. in diameter. In many areas the lining of both cysts consisted of stratified squamous epithelium.

Including the four cases presented by Shawan[43] a total of 11 proved cases of epidermoid cyst of the spleen have been reported. Other cases have been mentioned. Dinand, quoted by Shawan,[43] stated that Lubarsch had seen one case. Custer[9] reported five cases in 5,000 necropsies, but did not differentiate dermoids from epidermoids. The case reported by Emile-Weil, Roux-Berger et Scemama[12] has been reported by subsequent authors as another proved case of epidermoid cyst of the spleen. In the original article the authors stated that the stratified epithelium seen at first "recalls" stratified squamous epithelium, but proceeded later to describe in detail how unlike squamous epithelium it was. Montgomery *et al.*[34] reported a second case, but did not classify it as a true epidermoid cyst because it had been previously drained surgically. Lang *et al.*[27] reported a case in which the diagnosis of epidermoid cyst was made solely on the basis of pultaceous material removed from it.

DISCUSSION

The probable mode of origin of splenic cysts has caused much speculation. Numerous theories have been proposed, all of which have been reviewed by Fowler[16] and Shawan.[43] The most widely held opinions are those mentioned by Lereboullet[28] who felt that the cysts might arise from the inclusion of

germinal tissue capable of epithelial differentiation, and by Harding,[22] who thought the tissue was of endodermal origin. This endodermal tissue presumably may have arisen from inclusions of the perisplenium or of the peritoneum. Gosset[21] proposed that the pavement type of epithelium lining an epidermoid cyst arose as a result of metaplasia of the cells lining the splenic sinuses, and that trauma played an important role.

The following theory is presented on the basis of the observations made on the specimen presented in this paper. The finding of many small cysts about the large cyst, and of multiple, microscopic cystic spaces within grossly normal splenic tissue suggests primarily an embryonal defect in the organ. Their multiplicity may denote a multicentric origin. In some areas these cystic spaces coalesced due to pressure atrophy, giving rise to large cysts. The stratified squamous type of epithelium most probably arose from the inclusion of bits of the perisplenum which underwent an epithelial differentiation. No communication was demonstrated between the gross vascular tree and the cystic spaces, hence, one cannot ascribe a vascular origin to the cysts. For this same reason the flattened cells lining the small cystic spaces are probably of mesothelial origin rather than having their origin in vascular endothelium. The origin of splenic cysts and the stratified pavement lining which they possess is perhaps more logically explained in this manner than by assuming an inclusion within the spleen of the embryonal tissue primarily epidermoid in nature.

SUMMARY

Another case of epidermoid cyst of the spleen is presented. This brings to 11 the total number of such cases reported to date. The mode of origin of this type of cyst is discussed.

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SEGMENTAL ILEITIS; POSSIBLY CAUSED BY BACTERIUM NECROPHORUM*

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Bacterium necrophorum has been reported occasionally as a cause of disease in man but a search of the literature has failed to reveal any previous report of involvement of small bowel by this organism. Despite the fact that Dack, Dragstedt[1-4] and their co-workers have frequently demonstrated the presence of *Bact. necrophorum* in cases of chronic ulcerative colitis, Doctor Dragstedt informs me that he has no knowledge of any case in which involvement is of the small bowel. For this reason it was thought that the following case should be reported.

CASE REPORT

History. D. P., a white physician, age 57, entered the hospital on January 10, 1948, complaining of abdominal distention. He stated that he was in good health until January 1, when he suddenly developed postprandial distention. He had little nausea and no vomiting, but every time he ate solid food the distention recurred. He was able to retain a liquid diet but he noticed diarrhea of thin liquid stools which several times were of a black color. He noticed that his bowels moved after each time he drank liquid, so that it seemed to him that the fluids he took "went straight on through." There had been no fever, chills or abdominal pain and he had never noticed passage of blood, mucus or pus. Except for enucleation of an injured left eye in 1939 he had never been ill. His father died of heart disease at the age of 75 and his mother is living and well. There are no familial diseases to his knowledge.

Physical Examination. The patient was an obese, well-developed white male who seemed to be acutely ill. General examination was negative except for absence of the left eye and for moderate distention of the abdomen. Diffuse tenderness was present, particularly in the right lower quadrant and in the suprapubic area. Rectal examination revealed small external hemorrhoids and the impression of a firm, tender non-fluctuant mass in the right iliac fossa. Sigmoidoscopic examination showed nothing except a small adenoma at about 8 cm. above the anal verge. Barium and air contrast roentgenograms of the lower bowel were negative but the small bowel had the typical configuration of a partial obstruction.

Operation. Under pontocaine-glucose spinal anesthesia the abdomen was entered through a lower right rectus incision. The entire lower abdominal cavity was filled with extremely dense adhesions. Loops of the lower ileum were matted into one dense mass by these extensive agglutinations and the bowels could be dissected free only by slow tedious sharp dissection because of the denseness of the bands. In the region to the right of the sacral promontory an abscess cavity was encountered and about 30 cc. of thick yellow odorless pus spilled forth. This did not have the sulfur granule appearance of actinomycosis. Smears and cultures were immediately taken and the dissection was continued until the loops of small bowel were completely freed. The large and small bowel appeared to be normal except for an 8 cm. length of ileum approximately 60 cm. above the ileo-cecal junction. This segment was found to be badly inflamed, thickened and contracted. Because of the presence of the purulent abscess cavity and the poor condition of the

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patient a loop ileostomy, with the diseased segment of ileum forming the apex of the loop, was created. A Witzel ileostomy was created through the left flank, 5 Gm. of sulfathiazole was implanted into the peritoneal cavity and the abdomen was closed in layers with a Penrose drain extending down to the region of the abscess.

The patient was given 0.5 Gm. of streptomycin every 3 hours for 20 doses and 250,000 units of penicillin every 3 hours for 5 days, in addition to the routine postoperative treatment. The exteriorized loop of diseased ileum was removed 48 hours postoperatively. The Witzel enterostomy was, as is customary, working almost too well. The patient was dismissed from the hospital on his sixteenth postoperative day to complete his convalescence, during which time he was to take 2 courses of sulfadiazine before returning for closure of the ileum.

He returned to the hospital on April 24, 1948, and 3 days later operation was done under sodium pentothal and spinal pontocaine anesthesia. Inspection of the abdominal cavity revealed a remarkable clearing of the maze of adhesions previously noted. There was no evidence of any inflammation along the entire bowel; however for a distance of about 15 cm. to each side of the ileostomy loop the ileum was covered with a multitude of hard, pinhead sized, yellow masses which appeared to be subserosal. Because the nature of these was not clear I resected approximately 50 cm. of the ileum containing in its extent the miliary masses and the ileostomy loop. The remaining ileum was then restored by a side-to-side anastomosis.

The patient was dismissed from the hospital on his fourteenth postoperative day and is in good health up to this writing. He has regained his original weight and has no complaint except that rough foods tend to cause a temporary diarrhea.

Pathologic Reports. The cultures taken from the intra-abdominal abscess yielded a pure culture of an organism which had the morphologic and cultural characteristics of *Bacterium necrophorum.*

Microscopic examination of the specimen removed at the first operation was reported by Dr. Leo Lowbeer as follows: "Because of the fact that the loop was recently exteriorized and in addition a rubber tube was inserted through its wall, it is difficult to distinguish between the inflammatory reaction associated with this operation and that which may have existed prior to the operation. However the following statements can be made: the serosa of the exteriorized loop is covered with a thin layer of fibrino-purulent exudate which is being organized by very young granulation tissue apparently not older than a few days. This fresh, localized peritonitis is presumably the result of the recent exteriorization. Where the rubber tube had been inserted through the intestinal wall, all layers of the wall are severed and covered with a thin layer of fresh granulation tissue. This granulation tissue directly borders upon intact mucosa. These changes are also due to the recent operation. In addition, the mucosa and submucosa were for some distance replaced by a granulation tissue containing a large number of wide thin-walled capillary blood vessels. Underneath, the muscularis is densely infiltrated and at one point completely destroyed by inflammatory infiltration. Among the inflammatory cells, polymorphonuclear as well as mononuclear leukocytes were found. These changes seem to be of somewhat subacute character, perhaps of 2 weeks' duration. They indicate an acute to subacute ulcerative process of the intestine. In the neighborhood of this area marked fibrosis, round cell infiltration and consequent thickening of the submucosa were found, whereas the covering mucosa was intact. The underlying muscularis showed no evidence of fibrosis. The submucosal fibrosis is perhaps of longer duration than the ulceration of the adjoining mucosa-submucosa. Diagnosis: subchronic and recurrent acute to subacute ulcerative ileitis with early acute fibrino-purulent peri-ileitis."

Dr. Lowbeer's report of his microscopic examination of the loop of ileum removed at the second operation is as follows: "Submitted, a portion of the small intestine consisting of ileum and measuring approximately 50 cm. in length. At a distance of 12 cm. from one line of resection a double-barrel ileostomy is found surrounded by a strip of skin measuring 9 by 4 cm. The serosa of the intestine appears to be thickened either

diffusely or in the form of small nodules which frequently are hyperemic. These nodules do not have the gross appearance of tubercles. They measure between 1 and 2 mm. The mucosa throughout the entire ileum is smooth and the lumen wide. Microscopically the mucosa of the ileum shows no changes in any of the examined sections. The submucosa is somewhat edematous and shows a mild degree of round cell infiltration. In addition, many small subserosal nodules are found consisting predominantly of foreign body giant cells which are arranged around crystalline material which are easily detectable under polarized light. No definite statement can be made about the nature of this crystalline substance, but it may consist either of magnesium silicate as found in talcum powder, or of sulfa crystals. (Author's Note: Later examination of these crystals in the flame spectrometer revealed that the crystals were sulfathiazole.) Diagnosis: diffuse serosal fibrosis and multiple serosal foreign body granulomas."

COMMENT

The ability of *Bact. necrophorum* to invade a human host is again demonstrated in this case where the organism was isolated as a pure culture from an intra-abdominal abscess. The source of the abscess in the case recounted may be a fair matter for conjecture but the presence of an acute segmental ileitis in the absence of abnormality of any other segment of the large or small intestines is at least circumstantial evidence that *Bact. necrophorum* can be a pathogen of regional ileitis. Dragstedt *et al.*[4] believe that they have sufficient evidence to prove that *Bact. necrophorum* is one of the etiologic agents of chronic ulcerative colitis.

Schmorl[5] reported in 1891 the first recorded cases of human infection from the necrobacillus. He and an assistant contracted local lesions on their fingers while studying epidemic labial necrosis of rabbits. Shaw[6] managed to collect 22 cases from the literature. Stemen and Shaw[7] in 1910 recorded the first instance in which it was recovered in a pure culture from a human host by growing it from infected skin bullae of a meat-inspector, who had scratched his hand on a tooth of an infected sheep.

Dack *et al.*[2] maintain that the strains of *Bacterium necrophorum* show no clearcut differences from those of *Bacillus funduliformis* and since both lack the ability to form spores (which is characteristic of the genus Bacillus) they placed them together in the genus Bacterium, retaining the species name necrophorum on the basis of its priority. *Bacillus funduliformis* has been studied extensively by Prof. Lemierre of Paris, who has isolated it frequently from the blood stream of patients suffering from septicemia and peri-tonsillar abscess.[8-9]

Although there are steadily increasing reports of serious infections due to *Bact. necrophorum* a search of the literature failed to reveal any record of ileitis due to this or synonymous organisms.

CONCLUSION

In a case of intestinal obstruction due to an acute segmental ileitis an intra-abdominal abscess was found which contained a pure growth of *Bact. necrophorum*. Very heavy dosage of antibiotics and succinyl sulfathiazole resulted in complete eradication of the disease process.

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The Matas Award in Vascular Surgery

The fifth presentation of the Matas Award in Vascular Surgery was made to Dr. Alfred Blalock, Professor of Surgery at Johns Hopkins University, at The Hutchinson Memorial Building, Tulane University on January 17, 1950. The Matas Award was created by the establishment of the Violet Hart Fund in Tulane University. Previous recipients of the Matas Award have been Doctors Mont Reid, Raynaldo Dos Santos, Daniel Elkin and Robert Gross.

SYNOVIAL SARCOMA OF THE CHEST WALL*

REPORT OF A CASE

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IN 1944, HAAGENSEN AND STOUT[3] published a critical review of all previously reported instances of synovial sarcomata, including nine cases of their own. More recently, Bennett[1] has analyzed a large series of such tumors studied at the Army Institute of Pathology. In both publications it is pointed out that synovial sarcomata do not usually occur in joints, bursae, or tendon sheaths. However, all of the reported tumors of this type have been observed in the extremities or in the axillae,[2] groins,[1, 3] and buttocks.[5] The occurrence of a synovial sarcoma in the soft tissues of the chest wall seems worthy of presentation.

CLINICAL HISTORY

C. R., a white female, age 6 years, was admitted to the Hospital of the University of Pennsylvania on March 21, 1947, because of a tumor of the chest wall first noticed 2 weeks previously. The past medical history was not relevant. The only pertinent point in the family history was that a maternal uncle had been under treatment for Hodgkin's disease for the past 2 years.

On physical examination a soft, somewhat nodular, movable, non-tender subcutaneous mass was noted on the right anterior chest wall, overlying the costo-chondral junctions of the fifth and sixth ribs. The right submaxillary salivary gland was palpable, measuring approximately 2.5 cm. in diameter. It was firm, non-tender, and movable. A firm lymph node 0.5 cm. in diameter was detected in the left anterior cervical chain.

The results of routine laboratory studies were within normal limits and roentgen ray examination of the chest disclosed nothing to suggest metastasis.

At operation on March 22, 1947, (Dr. I. S. Ravdin) a firm, rounded, apparently encapsulated mass, approximately 4.0 cm. in diameter was shelled out of the subcutaneous tissues of the right anterior chest wall, between the rectus abdominis muscle and the costo-chondral junctions of the fifth and sixth ribs. The tumor was considered to be malignant on the basis of a quick frozen section examination, but exact diagnosis could not be made. Through a second incision below the mandible the right submaxillary salivary gland and several small surrounding lymph nodes were also removed (pathologic study of these disclosed no significant changes).

The postoperative course was uneventful and the patient was discharged on March 29, 1947.

No abnormalities were noted in a chest roentgenogram on May 8, 1947. On January 8, 1948, a small mass was noted by the child's parents on the anterior chest wall near the site of the previous operative procedure. Upon re-examination on January 18, 1948, there were noted 3 palpable subcutaneous nodules in the chest wall. One, 0.5 cm. in

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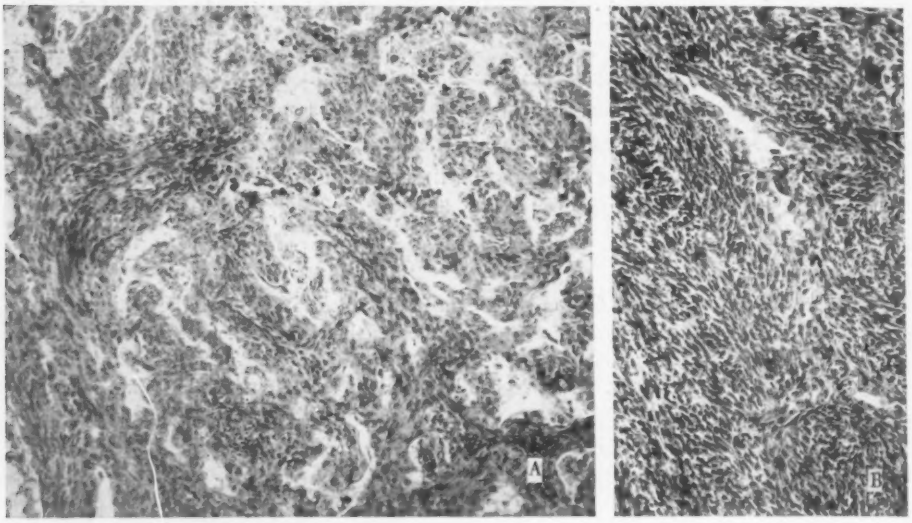
diameter, was situated beneath the superior pole of the scar. The other 2 nodules were medial to the scar.

The day after admission the scar of the previous operation was excised, together with a wide margin of surrounding skin (Dr. I. S. Ravdin). The underlying tissue, including part of the remainder of the rectus abdominis muscle, was removed en bloc. Convalescence was uneventful and the patient was discharged on January 26, 1948.

Again on June 14, 1948, a nodule was noted beneath the scar of the previous operation in the right subcostal region. This grew rapidly and when the patient was re-admitted to the hospital on July 1, 1948, the clinical dimensions of the mass were estimated to be 15 cm. by 8 cm. by 2 cm. The central portion of the mass was adherent to the overlying integument and its deeper aspect was fixed to the fifth and sixth costal cartilages. There were no other abnormalities and the results of routine laboratory studies were again within normal limits.



A B

FIG. 1.—Low power photomicrograph of primary tumor (x 95) hematoxylin and eosin stain. (A) Anastomatic sinusoidal spaces lined by large epithelium-like cells. (B) An area showing the spindle-celled portion of the neoplasm.

At operation on July 2, 1948, (Dr. I. S. Ravdin) the tumor, together with a wide margin of surrounding muscle, portions of the fifth, sixth, and seventh costal cartilages, and an ellipse of overlying skin, was removed en bloc.

The patient was discharged on July 14, 1948, after an uneventful postoperative course.

A nodule, presumed to be a recurrence, was noted just lateral to the upper end of the scar in April, 1949. Although excision was decided upon, the nodule disappeared before hospital admission could be arranged, and operation was deferred. The mass was again noted in September, 1949, and has persisted. After consultation, it was decided to try a course of chemotherapy. Five milligrams a day of A-methopterin given over a three-week period has effected no change in the recurrent tumor. The mass was resected by Dr. I. S. Ravdin on November 25, 1949.

Pathologic Description. (Surgical Pathology Nos. 57468, 62235, and 65368) The mass removed from the chest wall at the first operation measured 5 cm. by 4 cm. by 3 cm. It was composed of firm, homogeneous, yellow-gray tissue flecked here and there with hemorrhagic areas. The cut surface was indefinitely lobulated. On microscopic exam-

ination (Figs. 1 and 2) the tumor was seen to present two distinct pictures. Some portions were composed of bands of elongated cells, with large vesicular nuclei and prominent nucleoli. Elsewhere similar tissue composed a framework for innumerable anastomotic sinusoidal spaces. The latter were lined by large, rounded, polygonal, epithelium-like cells arranged in single or multiple layers. Focal proliferation of these cells not infrequently produced small tufts within the sinusoidal spaces. Many of the smaller spaces occurred as slits among the elongated cells, and were devoid of an epithelium-like lining. Wilder's silver stain revealed reticulin fibers in the spindle-celled areas, separating each cell from every other cell, whereas such fibers were not found among the rounded, polygonal cells lining the sinusoidal spaces. Abundant mucicarminophilic material was demonstrated within these spaces by appropriate staining. The neoplastic cells exhibited

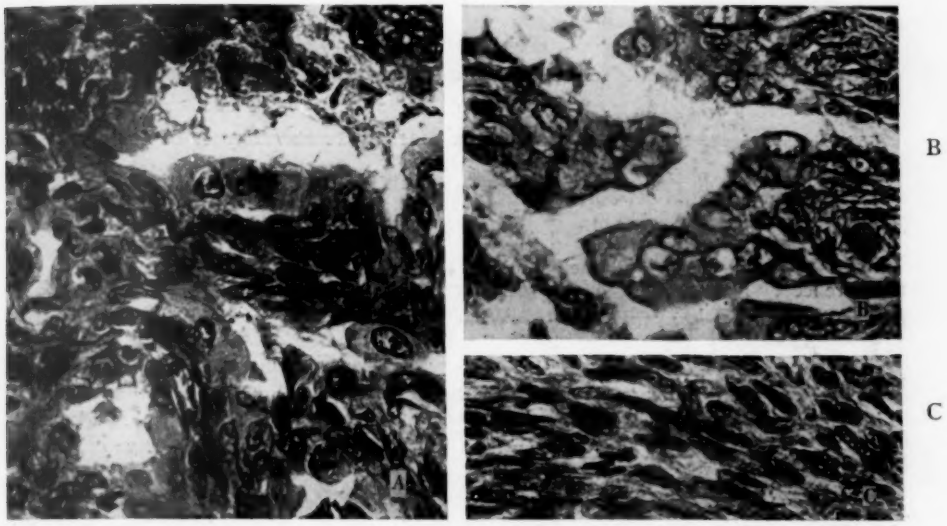


FIG. 2.—Higher magnification of primary tumor (x 460).

(A) Shows details of the large, polygonal lining cells which merge with the underlying spindle-cell framework (hematoxylin and eosin).

(B) Reticulin fibers are abundant in the spindle-celled areas, but absent between the epithelium-like lining cells (Wilder's reticulin stain). (C) Details of the spindle-celled portion (hematoxylin and eosin).

moderate pleomorphism, and mitotic figures averaged one in every two to three high-power fields.

The gross specimen removed at the second operation contained three definite nodules, ranging in size from 1 to 1.5 cm. in diameter. These were firm, light yellow and were embedded in fibro-fatty tissue.

Histologically (Fig. 4-A) the nodules were composed of interlacing bundles of fusiform cells. The spaces which were a conspicuous feature of the original tumor were not so numerous, and lacked the epithelium-like lining cells. However, the recurrent tumor resembled the spindle-celled element of the original very closely and there seems to be no reasonable doubt that they represent the same neoplasm.

The specimen removed at the third operation consisted of a mass of muscle tissue, portions of three costal cartilages and a strip of peritoneum, forming a mass measuring 11 cm. by 9 cm. by 3.5 cm. overall. This was surmounted by a 12 cm. by 2 cm. skin ellipse which encompassed the scar of the previous (second) operation. A firm, irregular, pale yellowish-white tumor, measuring 5 cm. by 4 cm. by 3 cm., lay between the resected

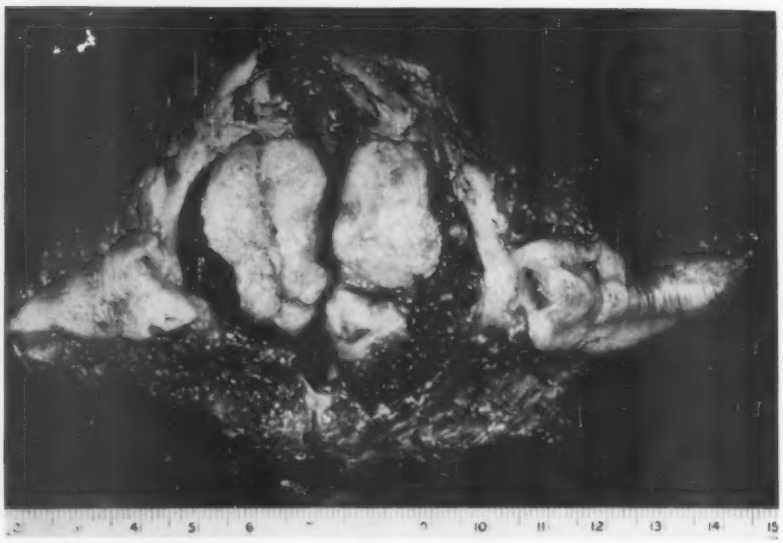
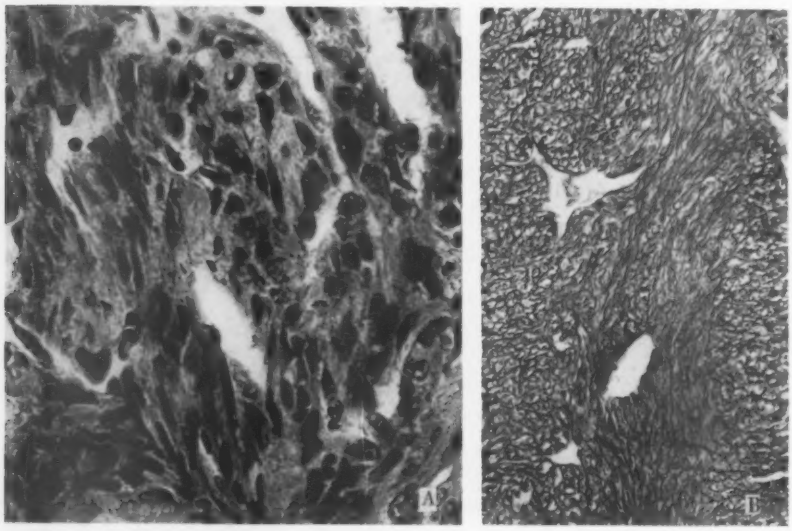


FIG. 3.—Gross specimen removed at the third operation (second recurrence). The tumor and overlying skin ellipse have been sectioned transversely. Much of the tumor is enveloped by a definite capsule.



A B

FIG. 4.—Photomicrograph of recurrent tumor, showing similarity to the spindle-celled areas of the original. (A) (x 460), hematoxylin and eosin stain, tumor removed at the second operation (first recurrence). Bands of elongated cells enclose slitlike spaces devoid of epithelium-like lining cells. (B) (x 100), Wilder's reticulin stain, tumor removed at the third operation (second recurrence). Abundant reticulin fibers separate each cell from every other cell.

muscle and costal cartilages, and was adherent to these structures at several points. Elsewhere the tumor was enveloped by a delicate capsule (Fig. 3).

Histologically (Fig. 4-B) the tumor was composed of interlacing bundles of uniform elongated cells, closely resembling the tumor removed at the second operation and the spindle-celled portions of the original tumor.

COMMENT

Before concluding that this neoplasm was a synovial sarcoma the possibility was considered that it might have taken its origin from pleural or peritoneal lining cells, or from vascular endothelium. Since the tumor bore no anatomic relationship to either pleura or peritoneum, mesothelial origin seems unlikely.

Haagensen and Stout[3] have remarked upon the morphologic similarity of the synovial sarcoma and the hemangioendothelioma, pointing out that they may be distinguished by the latter's inability to produce a mucicarminophilic substance. The tumor herein reported contained abundant material which was stained with mucicarmine.

As Haagensen and Stout[3] have stated, the synovial sarcomata do not appear to be derived from the normal lining cells of joints, bursae, and tendon sheaths. The fact that tumors having the characteristics of the synovial sarcomata arise at sites far removed from regularly occurring synovium-lined structures suggests that synovial sarcomata are a neoplastic expression of the ability of the supporting tissues of the body to form synovium-lined spaces under certain conditions. The transition of connective tissues to synovium-lined structures is reported by Key[4] and Wolcott[9] following synovectomy in animals. The formation of adventitious bursae, which may be indistinguishable histologically from those occurring regularly, is further evidence of this potentiality.

The synovial sarcomata may be but another expression of the versatility of mesenchymal tissues when undergoing neoplasia, as well as in normal development. Instances of this are provided by the occurrence of extraskeletal osteogenic sarcomas, examples of which are reported by Wilson,[8] and by Sugarbaker and Ackerman.[7] Stout[6] emphasizes this versatility of the primitive mesenchyme in accounting for a group of mixed mesenchymal tumors which he has recently described under the name of mesenchymoma.

SUMMARY

A synovial sarcoma, arising in the soft tissues of the chest wall of a six-year-old white female, is reported. The tumor has recurred locally twice within the 16 months following primary resection.

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Editorial Address

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ANNALS OF SURGERY

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Editorial . . .

The Necessity for Accurate Evaluation in Surgery

Since the birth of medical science the problem of evaluation of data and thought in the development of our profession has been ever-present. The difficulty in separating the good from the bad has increased in recent years because of the increased number of "new ideas," which naturally has resulted in much indecision in the mind of the expert, as well as the student of medicine. Perhaps the greatest errors are made in premature acceptance of new ideas, because all of us are anxious to be as progressive as the other fellow, and not miss any opportunity to improve. Medical journals and books are possibly of greater importance than other factors in the danger of misrepresentation or distortion of facts, because ideas which have been given sufficient thought to be put into print are supposed to have merit and stand the test of time.

This extreme difficulty in discriminating properly should impress upon us the need for very close scrutiny of all new ideas, but we must not forget the need for generosity in our interpretation of values. The fact that the great discovery of penicillin was dependent upon the seemingly insignificant observation that a fungus obliterated a colony of pyogenic bacteria on an agar plate, should convince any skeptic that almost any research containing true factual data may be the stepping stone toward an important discovery if proper intelligence is utilized in studying and assimilating it.

However, the generosity suggested above in judging the merit of data must be applied with caution, because we know from past experience that too many new ideas which are accepted at the time of their presentation as truths, later are shown to be false; if practiced, these may result in no benefit or even great harm. For example, the suggestion made many decades ago to pour boiling oil into a freshly inflicted wound to sterilize it, or prevent infection, was accepted rather widely; yet, it is obvious that the harm done the tissues subjected to this vicious therapy was incalculable. To make this axiom—"not all new things are truths"—more emphatic let us recall that not so many years ago the injection of varicose veins was accepted almost universally as a great advancement, and for a time displaced vein stripping and most other procedures as a method of treating varicosities. After trial and error convinced us that injection of varicose veins was followed by a large percentage of failure we ventured upon another trial and error experiment in which ligation of the offending vein was practiced almost in a wholesale manner. Now we know that ligation has marked limitations, and that the seemingly obsolete procedure of stripping varicose veins was not so ineffective after all.

Judging from past experience we must assume that many operations as well as non-operative procedures now considered valuable will be abandoned, some because they will be displaced by better procedures, and some because experience will expose them as ineffective and perhaps even harmful. Even such a valuable contribution as portacaval anastomosis has disturbing elements surrounding its use, in so far as the mortality from the operation is high, and

recent data support the contention originating years ago that an Eck's fistula may interfere with hepatic function, as indicated by studies on liver function tests and nitrogen metabolism.

Centuries ago surgery was primarily an art. In fact, it can be said that only during the past six or eight decades has science played a significant rôle in our specialty. Unquestionably, the application of scientific methods, such as the proper utilization of physiologic and chemical principles in pre- and post-operative care, has been responsible for our ability to perform major operations with satisfactory results, particularly with regard to mortality rate. Improper evaluation of a patient's physical reserve as related to ability to withstand a given operative procedure has been responsible for many deaths indeed. Unfortunately, there is no possibility of constructing a machine into which physiologic and chemical data may be inserted for calculation into a mathematical answer on mortality and morbidity. However, an approximation of these factors must be obtained, and can be achieved only by intelligent consideration of data, being careful to utilize all information obtainable.

Actually, mathematical principles must be utilized before decisions on many controversial procedures can be made. For example, it would be bad judgment indeed to perform an operation which would be associated with a 75 per cent possibility of death (in a poor risk patient) when survival following operation would perhaps be increased merely from an expected interval of two years without operation to two and one-half years with operation. The contra-indication for operation in the above case is very clear cut. Unfortunately, the surgeon is confronted almost daily with similar problems but with a solution much less obvious. Correct interpretation is made more difficult by the fact that a calculated mortality rate for a given operative procedure cannot be used in every patient, because it may be 50 per cent in one patient and three per cent in another. It is only by complete and intelligent study that a fairly accurate estimation of mortality in a certain patient can be achieved; after the dangers of the operation are properly evaluated, the surgeon must ask himself just how much improvement in the patient's welfare will result from the operation. Too often indeed, the surgeon gains the impression that his surgical efforts have been followed by a cure, perhaps because the patient's convalescence was unmarred by complications or serious symptoms. Only by careful follow-up of many patients can we obtain an accurate estimation of how much improvement may be expected in a certain patient following a certain operation.

Accordingly, this editorial is presented as a plea to secure the maximum amount of data available on our patients and to evaluate it with maximum accuracy, because nothing in this world is more important than life and health. Likewise we should remember that "not all things new are truths." We must not blindly adopt a new procedure or new operation without a complete survey of its dangers as well as advantages. When it is impossible, by study of available data, to arrive at a conclusion, then one must obtain that data from experience, but large numbers of patients must not be subjected to procedures of unknown value until results in a small number justify it.

WARREN H. COLE.